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THE HISTORY AND PRESENT-DAY USE OF ERGOT*

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AMONG THE MANY epidemics of disease that ravaged Europe in the Middle Ages there was one with outstanding features. It caused a tingling of the skin and great pain as of burning. Fingers, toes and even whole limbs turned black and were cast off. In certain circumstances convulsions occurred, and these, linked as they were with mental frenzy and hallucination, may explain some of the "dancing epidemics" that have long puzzled historians. Cattle suffered as well as man, and—significant to our story—pregnant sows littered before their time.

As early as the year 945 a plague of "the fire" occurred in and around Paris. Sufferers flocked to the church of St. Mary, where, we are told, they received a daily ration of food; when however they returned home some found that "the quenched fire was rekindled." At a later date a brotherhood of monks dedicated to St. Anthony established hostels in the stricken areas, and probably because of this association the disease came to be called "St. Anthony's Fire." The historical basis for this name is however obscure, and the term has also been loosely applied to diseases such as erysipelas.

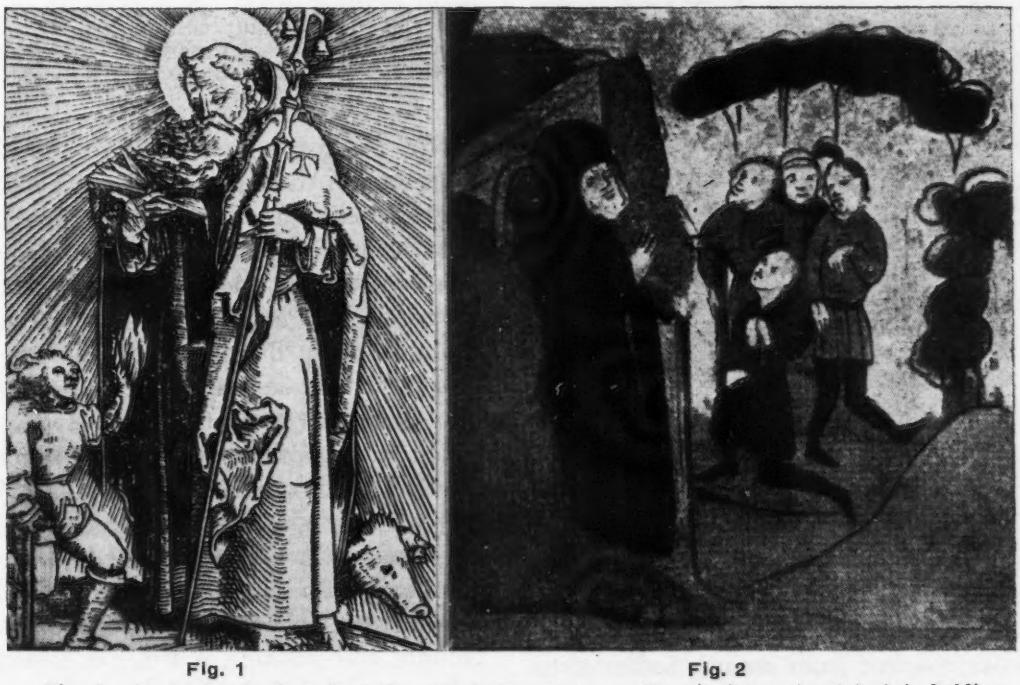

Fig. 1 Fig. 2

Fig. 1.—An early woodcut depicting St. Anthony. A suppliant (with maimed leg) is holding up his hand, which is enveloped in a symbolic fire. **Fig. 2.**—A fresco from the church at Waltalingen in S. Germany. The suppliants show the limbs in abnormal positions—a characteristic of the convulsive form of ergotism.

This strange and often fatal illness occurred chiefly in the corn-producing districts of South Germany and France where rye was grown in preference to wheat. The disease appeared only in certain years, and probably only in wet seasons for it is then, as we now know, that the rye is commonly affected with a fungus which appears in the head of the grass as black, slightly

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Canad. M. A. J.
May 15, 1955, vol. 72

Fig. 3.—An early representation of St. Anthony, surrounded by crippled sufferers. Hanging from the rail are cast-off hands and feet, or reproductions of such relics.

curved spurs, three or four times the length of the natural grain.

Who first attributed the "cold fire" to the eating of bread made from diseased rye is not known; but it is certain that by the 16th century the danger of secale, or ergot of rye, became recognized. More of interest to us now would be to know who first associated the eating of the diseased rye with the forcing of the pains of women in childbed; but whom we should name and whom honour is likewise lost from record. Suffice it to say that by the year 1582 there was documentary record of the medicinal use of ergot. Lonicer, describing the ergot spurs in diseased rye, goes on to state, "they are held to be a special medicine for women in labour, and for the purpose of awakening the pains three of the spurs are swallowed." This precise dose, recorded so many years ago, is of more than passing interest for, to jump far ahead in our story, three of the ergot spurs contain, on the average, one half-milligramme of ergometrine, the dose of the pure alkaloid now used in obstetric practice.

During the seventeenth and eighteenth centuries the midwives of certain regions of France and Germany were well acquainted with the use of ergot for hastening "lingering labour." The knowledge was doubtless passed from mother to daughter; and there is record that the drug was given in powder form, dispensed in some cases from a coffee-mill.

For the next chapter, our story turns abruptly to Saratoga County in New York State where Dr. John Stearns, a country practitioner, long importuned by a midwife with whom he worked, had made use of a powder prepared from the black corns found in a rye granary. How astonished he was by the result may be judged by a letter which was published some months later. This letter, destined to become famous, contained the following sentences:

> "Previous to its exhibition it is of the utmost consequence to ascertain the presentation as the violent and almost incessant action which it induces in the uterus precludes the possibility of turning . . . . you will be surprised with the suddenness of its operation; it is, therefore, necessary to be completely ready before you give the medicine."

This publication marked the introduction of ergot into orthodox medicine. The use of the drug quickly spread, and is frequently referred to in the medical journals of the time. But trouble soon arose. Practitioners failed to realize the danger of the "almost incessant action which it induced"; they did not heed the warning that "turning was precluded"; and many lacked sufficient judgment to distinguish between a labour which was merely slow and one which was obstructed. The result was inevitable. The drug was wrongly given; many a fetus was stillborn, and many a mother succumbed to a rupture of her uterus. As so often happens when opinion is wavering, an apt phrase turned the trend of thought and practice. A letter in a medical journal proposed that the *pulvis ad partum*, as ergot had been called, should be renamed the *pulvis ad mortem*. This cynical remark arrested attention; the danger of ergot was recognized, and by the end of the century its use during labour had been virtually abandoned. But not so its use in the control of hæmorrhage after delivery: for this purpose ergot continued to be highly prized, and has gained in importance to the present day.

EARLY CHEMICAL WORK ON ERGOT

The 19th century saw the development of the modern science of organic chemistry. In the

field of pharmacology an early success was the extraction from certain crude drugs of pure chemical entities with properties identical to those of the parent substance. Notable in this respect was the isolation of morphine from opium—an achievement then regarded with astonishment, for Nature's secrets were too complex, so it had been supposed, ever to be unravelled. With this and similar successes in hand it was natural that the chemist should turn his attention to the ergot of rye which also had remarkable medicinal properties. The undertaking was to prove unexpectedly long and difficult but, as if by way of compensation, many rich fields for new research were to be laid open for those with eyes to see.

To elaborate. The investigation of the fungi, as distinct from the green forms of plant life, involved the study of new classes of chemical substance. A notable example was the steroids; and much of our present-day understanding of the chemistry of this group of substances is the outcome of the early work on ergot. Direct links can thus be established between ergot research on the one hand and our modern knowledge of sex hormones—to mention only one class of steroids—on the other. And the connection goes further; irradiated ergosterol links ergot with vitamin D research, while other modifications of the essential sterol nucleus link it with the most modern work on cancer-producing substances.

By yielding up the sterols the bounty of ergot was only touched. Early search for the principle which caused uterine contraction led to false pursuits but also to unexpected rewards. Familiar and highly important substances such as histamine, tyramine, and even acetylcholine, were—strange as it may now seem—first discovered in ergot, or were first adequately studied in consequence of their discovery in ergot.

To anticipate now the development of the main story, not least important among the incidental discoveries was Dale's finding that ergotoxine—the first active alkaloid to be extracted from ergot—had the property of abolishing the motor effects of sympathetic stimulation and of adrenaline. The existence of inhibitory fibres in the sympathetic innervation of the blood vessels was thus brought to light, and the peculiar phenomenon of the reversal of the action of adrenaline was discovered.

It is interesting to record that this observation was accidental. A cat had failed to show the

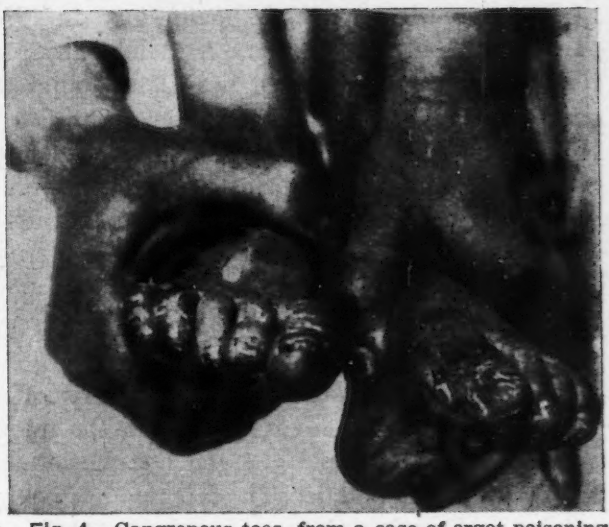


Fig. 4.—Gangrenous toes, from a case of ergot poisoning occurring in the 20th century. (Barger: *Ergot and Ergotism.*)

Fig. 5.—Ergot spurs growing on rye grass.
Figs. 3 and 5 from A. Stoll, Berner Naturforschenden Gesellschaft, Dec. 1942. (Verlag Paul Haupt, Bern.)

customary pressor response to adrenaline—a substance then newly marketed, and standardized by biological assay. Dale at first concluded that this particular sample must be inactive; but when, a week later, a further sample again produced a fall instead of a rise of blood pressure his suspicions were aroused. In searching for an explanation he observed that both the cats used had previously received a large dose of an ergot extract (the extract which was later to yield ergotoxine). This fact, acting on an enquiring mind, prompted a long series of experiments, the result of which was to establish the existence of a specific vasomotor reversal effect which, as we know, is peculiar to a group of ergot alkaloids. This discovery has been of outstanding importance to physiologists for it has enabled them to unravel some of the intricacies of sympathetic and of parasympathetic innervation.

Canad. M. A. J.
May 15, 1955, vol. 72

Let us return now to the main story. In 1878 Tanret obtained from ergot a crystalline alkaloid ergotinine, which, however, was later found to be devoid of activity. Success seemed far away. But in 1906, Barger and Carr in London isolated another alkaloid, ergotoxine—later to be prepared in greater purity and in crystalline form*—which undoubtedly stimulated the isolated uterus, and which, if long administered in heavy dosage, also reproduced the gangrene-producing properties of the parent drug.

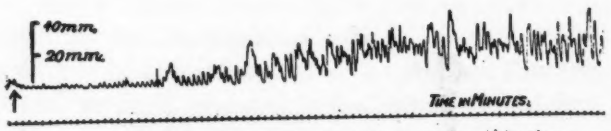
In 1918 Stoll announced the discovery of a new alkaloid ergotamine which, under the trade names of Femergin and Gynergen, became widely used in obstetric practice. The fact that it quickly attained clinical eminence has been cited as evidence of superiority over the older ergotoxine; but a more probable reason is that it had the backing of more effective publicity by the parent manufacturing company.

For a time there was doubt whether these two alkaloids might not be one and the same substance, but later investigations clearly established their separate chemical identities. The biological effects of the two alkaloids were, however, very similar and, as I was later able to show, their actions on the human puerperal uterus were indistinguishable. I should now like to explain in greater detail this work of more than twenty years ago, and I ask your indulgence if I now continue the story in somewhat personal terms.

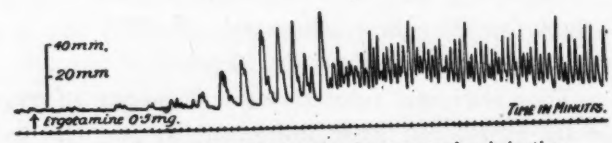
CLINICAL TRIALS OF ERGOT DERIVATIVES

In consequence of discussions regarding the rival merits of ergotoxine and ergotamine, the Medical Research Council, through their then recently organized Therapeutic Trials Committee, approached my late chief, Professor F. J. Browne of University College Hospital, London, and proposed a careful clinical trial of the two drugs. Professor Browne invited me to undertake this research, and together we discussed possible methods. Most of these were dismissed as unlikely to be sufficiently certain in their results. Only one gave promise of success. This was the mechanical recording of intrauterine pressure of a woman in labour by a method then recently described by Bourne and Burn.[1] Attractive as this was, it had the apparently insuperable objection that the ergot alkaloid would have to be administered to a parturient woman with risk to herself and to her unborn child. At this stage I recalled how easy it was when making a routine post-natal examination to insert the finger into the still open uterine cavity: what was possible for the finger should be possible for a small recording bag. There might be danger of introducing sepsis; but this was regarded as remote if the end of the first week were chosen when a leukocytic barrier in the uterine wall would be well established. After careful consideration, this was the method adopted. The results achieved with it exceeded my highest expectations; the puerperal uterus was found to be, in fact, an ideal test organ. At a much later date a method of external recording was substituted for the use of an intrauterine bag; but this, though satisfactory for many purposes, never gave the precision of the original method.

To return now to the work on ergotoxine and ergotamine. Here were two alkaloids which together apparently provided the answer to ergot's secret. But did they entirely do so? Undoubtedly they stimulated the uterus, but their action was slow; twenty minutes elapsed after intramuscular injection before any effect was seen, and when administered by mouth the delay was well in excess of two hours. Let us now turn back to John Stearns's letter. In it we read: *"The suddenness of its action* [i.e. the administration by mouth] *will surprise you."* This could only mean that the effect took place within a matter of minutes. By this token, neither alkaloid had an action which measured up to the "Dr. John Stearns effect." Only one explanation was possible. Ergot must



Ergotoxine 0.5 mg. by intramuscular injection.



Ergotamine 0.5 mg. by intramuscular injection.

Fig. 6.—Tracing from the human postpartum uterus showing the effect of ergotoxine and of ergotamine after intramuscular injection. Note the long delay in the onset of effect (20 minutes or more); when given by mouth the delay was in excess of two hours.

*In more recent times, Stoll of Basle has shown that ergotoxine has a strong tendency to form loose combinations with two or more similar alkaloids. He has therefore proposed that the term ergotoxine should be used to denote the group; and that the particular alkaloid to which it was previously applied should be renamed "ergocornine." This proposal, however, does scant justice to the original discoverers of ergotoxine; and certain other workers have deprecated the alteration of the original nomenclature.

contain another active substance, or other substances, which had as yet eluded detection. If I may use a metaphor—but without any intent to disparage my colleagues—I might say that the pharmacological dogs had been so absorbed in barking at the cats in the tree in front that they had missed a bigger and altogether more delectable kitten sitting in the tree behind.

I should be happy were I able to say that this was the reasoning that occupied my mind at that time, but I confess that the discovery now to be mentioned was in fact more or less accidental. Having examined the two alkaloids mentioned, it was natural to pass on to the examination of other oxytocic or allegedly oxytocic substances, and an obvious first choice was the aqueous extract of ergot which was then official in the British Pharmacopœia but which had been condemned by many authorities for the reason that it contained neither ergotoxine nor ergotamine.[2]

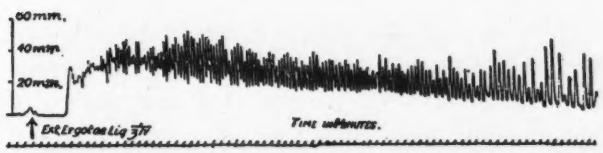


Fig. 7.—The effect of liquid extract of ergot (B.P. 1914) given by mouth to a puerperal woman. Note the suddenness of the action (4½ minutes in this case).

The first recording with this old and much criticized preparation was indeed memorable. As I watched the needle mount higher and higher, my first reaction was that a fault had developed in the recording apparatus. My next was that the patient must be behaving in some unprecedented manner—but no, a quick inspection of the woman as she lay in the adjacent room showed that she was, in fact, calmly eating her lunch. My third and lasting impression was one of sheer astonishment. "Then felt I like some watcher of the skies, when a new planet swims into his ken."

Leaving my work, and with a mind still full of wonder, I made my way home. Then there flashed on me the true meaning of Dr. John Stearns's words. I realized that I had stumbled on the long-forgotten "Dr. John Stearns effect."

In retrospect, it is strange that the quick action of the aqueous extract had not been recognized before, for any patient observer by placing and keeping his hand over the puerperal uterus can detect the change caused by the drug. But such clinical observations as had previously been recorded had been vague, unconvincing, or soon forgotten.

THE ISOLATION OF ERGOMETRINE

Sir Henry Dale, then Director of the National Institute of Medical Research and member of the Therapeutic Trials Committee, who had greatly helped and encouraged me in this research, was now informed of the discovery. He had long suspected that ergot held further secrets and he reacted with characteristic enthusiasm. At once a research chemist in the Institute was pressed into service. This was H. W. Dudley, with whom I was soon to work in close and happy association. It is, however, sad to have to add that less than four years later—and, strangely on the very day when his full report on the chemistry of his newly discovered principle was published—Dudley was to succumb to a fatal illness.

At first our task seemed easy; but, through an assumption that the rapidly acting principle was probably a simple amine, much valuable time was lost. Later, it was realized that the principle was in fact an alkaloid, although remarkably small in molecular size and with solubilities distinctly unusual in this class of substance.

Much work was demanded. Unlike almost any other drug that has been isolated in pure form, there was neither chemical nor animal test by which its presence could be detected. Each successive fraction—and there were many scores of them—had to be examined by the only method available, the administration to a puerperal woman and the subsequent graphic recording of the behaviour of her uterus. Unexpected difficulties were encountered. Each new batch of raw ergot had to be tested for potency before being subjected to fractionation. More than once the supplies ran out, and we had to nurse our patience till a new harvest arrived from Spain. Many of the fractionations involved the use of highly toxic substances, and it is to Dudley's great credit that by scrupulous care he was able to eliminate all trace of these agents before the fractions were submitted to test. All the known precipitants—the heavy metals, the picrates and the rest—were pressed into service; and all the usual solvents were employed to fractionate the stubborn solids. Almost at once a remarkably high degree of purification was achieved; but not for nearly three years did final success seem to be at hand.

Shortly before Christmas Eve, 1934, I heard Dudley's voice on the telephone; he seemed strangely excited. A beautiful crystalline substance had made its appearance. Surely it must

Canad. M. A. J.
May 15, 1955, vol. 72

be the sought-for principle. It was tested. It was quite inert. It was a poor Christmas for both of us. But in the next few days another pure, crystalline substance was forthcoming, and from various chemical reactions that had now been evolved it promised to be of more than ordinary interest. A quick method of external recording was employed. The preparation was active. Another few days, and, on February 9, 1935, a beautiful tracing by the internal method was obtained. The new crystals had reproduced a perfect John Stearns effect.

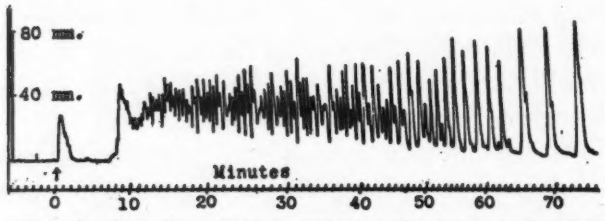


Fig. 8.—The first tracing made by the intrauterine bag method showing the action of the newly discovered alkaloid later to be called ergometrine. A perfect "Dr. John Stearns effect" was reproduced.

A council was held with Sir Henry Dale. Publication of the results would be delayed a few weeks to ensure that the chemical features could first be worked out with full accuracy. The method of preparation would be published in full. No patent rights or proprietary interests would encumber the new drug; it would be free for any manufacturing firm to produce. The name would be *Ergometrine*. All this came about, and the first announcement of the new alkaloid appeared in the *British Medical Journal* of March 1935.

Meanwhile, in other centres similar work had been in progress. Following the previous announcement of the discovery of a rapidly acting, water-soluble principle in ergot, various groups of workers pressed on with the chemistry of the drug. In 1932 in the course of a visit to Baltimore and later to Chicago, I had been able to repeat some of my original experiments on ergot and to interest clinicians in these centres in my methods of recording. By a strange coincidence, after a lapse of three years, an almost simultaneous announcement was made from three centres—from Baltimore (by Thompson[3]), from Chicago (by Kharasch and Legault[4]) and from Basle (by Stoll and Burckhardt[5])—of the isolation of a new, water-soluble ergot principle. The relationship of these various substances was fully discussed in the *British Medical Journal* of December 7, 1935. As might be supposed, all of them were soon found to be identical.

Of the alkaloid isolated in pure form in London it can be stated that it was the first to have its chemical characteristics adequately described so that the substance could be recognized by other workers, the first to have its method of preparation explained, and the first to be free from all possibility of commercial exploitation. One result of this multiplied work and multiplied discovery —in many ways a most useful development—was the confusion of names which soon arose. Some of these have passed from use; but in the U.S.A. the name which was eventually adopted for official use was "ergonovine"; and now a well-known proprietary name is "Ergotrate." In Switzerland the Sandoz firm has retained Stoll's name of "Ergobasine"; but in Europe generally, and throughout the British Commonwealth, "ergometrine" is the name employed.

THE USE OF ERGOMETRINE IN OBSTETRIC PRACTICE

How has the isolation of the pure alkaloid benefited obstetric practice? So far as the routine administration of ergot after the completion of normal delivery is concerned, the answer is, not at all. Simpler and much more economical is the old established custom of administering a teaspoonful of the liquid extract after the birth of the placenta. But, by contrast, when hæmorrhage from a relaxed uterus is concerned, there is an immense advantage in the use of the pure alkaloid, for it can be given by intravenous injection with the certainty of an almost immediate action on the uterus, and yet with complete freedom from undesirable side-effects on the patient. To this end, 0.25 to 0.5 mgm. is the dose employed (this is better than the smaller 0.125 mgm. dose originally proposed when lack of experience necessitated a cautious recommendation). Another obvious advantage of the pure alkaloid is that the injection can be given to the unconscious patient, or to the patient who is still vomiting after anæsthesia. So successful has this use of ergometrine become that the more dangerous pituitary extract has now been almost abandoned for this particular purpose.

A further use of ergometrine is the routine intravenous administration of the drug with the appearance of the fetal shoulder in order to bring about an almost immediate expulsion of the placenta after the birth of the fetus. I do not intend to go into the pros and cons of this practice save to state that the procedure, which

was first proposed by Davis of Chicago, is rapidly growing in favour. The results recently reported by Lister,[6] and by Martin and Dumoulin[7] and others—results which have been paralleled in my own Department—compel a reconsideration of the time-honoured method of managing the third stage of labour.

TABLE I.

RESULTS OF INTRAVENOUS INJECTION OF ERGOMETRINE GIVEN WITH BIRTH OF THE FETUS

	Number	*Hæmorrhage over 20 ounces (per cent)*	*Manual removal of placenta (per cent)*	*3rd stage less than 20 minutes (per cent)*
Controls				
Lister.....	762	16.0	2.2	80.2
Martin and Dumoulin..	1,000	13.1	1.1	62.0
Ergometrine series				
Lister.....	835	0.5	1.6	90.1
Martin and Dumoulin..	1,000	1.2	3.0	94.3

There can be no doubt that ergometrine, especially when employed by intravenous injection or by direct injection into the uterine wall, has greatly lessened the danger of postpartum hæmorrhage. This is reflected in mortality figures. The extent of the effect is, however, difficult to measure for it is necessary to recall that, simultaneously with the widespread use of ergometrine, came the much freer and more rational use of blood transfusion. Especially was this so in Britain, where, under the stimulus of war needs, blood banks were established in almost every hospital, and blood became freely available for obstetrical as well as general surgical use. It is also necessary to remember that the death rate in maternity work generally had sharply fallen because of a variety of other favourable factors, notably the advent of the sulphonamides and penicillin. Keeping these qualifications in mind, let us now turn to the Registrar-General's statistics for England and Wales. These show that the death rate from postpartum hæmorrhage had, for many years, remained virtually unchanged at about 0.3 per 1,000 live and still births. In the year 1940, however, it started to fall, and by 1952 (the last year for which records are available) it reached an all-time low record of 0.06 per 1,000 live and still births. Thus, for every five women who died from this cause in the earlier years, only one died in the last-mentioned year.

Such then is the clinical side of the story. Few drugs can have become so firmly established in so short a time, and few drugs can be so completely indispensable as ergometrine now is.

FURTHER CONSIDERATIONS OF CHEMISTRY

Let us now turn again to the chemistry of ergot. Much work has been accomplished since ergometrine was isolated. Other alkaloids have been identified, although these are of scientific rather than clinical interest. The more accurate knowledge which has now been gained enables the alkaloids to be arranged in groups in order of complexity. Ergometrine is by far the simplest, and is peculiar in containing no pyruvic acid. The ergotamine group contains pyruvic acid and an amino acid. The ergotoxine group contains dimethylpyruvic acid and an amino acid. All these alkaloids are built on a complex molecule named lysergic acid, which itself is biologically inactive. Lysergic acid exists in two isomeric forms, and on each of these is built a series of alkaloidal isomers, one lævo-rotatory and the other dextro-rotatory. Only the lævo-rotatory series is biologically active. It is interesting to recall that, as mentioned earlier in this paper, ergotinine, the first ergot alkaloid ever to be isolated, was biologically inactive; it belonged, as we can now see, to the dextro-rotatory group.

TABLE II.

Lævo-rotatory	*Dextro-rotatory*
Ergocristine	Ergocristinine
Ergokryptine	Ergokryptinine
Ergotoxine	Ergotinine
	ψ Ergotinine
(Ergocornine)	(Ergocorninine)
Ergotamine	Ergotaminine
Ergosine	Ergosinine
Ergometrine	Ergometrinine
All the above are built on lysergic acid	All the above are built on *iso*lysergic acid

And still the story is not ended. By brilliant work in chemical synthesis Stoll has produced a series of semi-synthetic alkaloids. Working with lysergic acid (which is common to all the alkaloids mentioned) he was able to introduce several different side groupings which bestowed on the inert substance an ergometrine-like activity. One of these is marketed under the name of Methergin and is now in clinical use. Gill,[8] work-

Canad. M. A. J.
May 15, 1955, vol. 72

ing in my Department, has shown that in most respects it is at least the equal of ergometrine, failing only to reproduce in quite the same degree the latter drug's remarkable rapidity of action.

By hydrogenation of the lysergic acid portion of the molecules Stoll has produced another series of modified alkaloids which, in the case of members of the ergotamine and ergotoxine groups, possess enhanced sympathicolytic properties but reduced or abolished oxytocic properties. Dihydroergotamine (D.H.E. 45) is the best known example, but a mixture of these alkaloids is also marketed under the name of Hydergine. These drugs are much used in the treatment of migraine and greatly shorten the duration of an attack. Garrett,[9] working in my Department, has thrown some doubt on their mode of action, for the concentration theoretically necessary to paralyze sympathetic nerve endings is not attained in the dosage permissible in clinical work. Rather surprisingly, he has also found that, with regard to the behaviour of the intact human uterus, dihydroergotamine has an oxytocic action indistinguishable from that of ergotamine, save only that it is less powerful. The use of dihydroergotamine in labour is therefore accompanied by a similar risk of uterine spasm similar too that associated with the use of the naturally occurring active ergot alkaloids.

By yet another modification of the lysergic acid portion of the molecule—this time of ergometrine (ergobasine)—Stoll has produced a new compound which strangely disturbs the higher cerebral centres. This drug, lysergic acid diethylamide, is now being cautiously employed in the assessment of certain psychiatric states.[10]

These many and varied alterations of the naturally occurring alkaloids, together with the consequent alteration of their mode of action, are of very great scientific interest, and furnish a remarkable example of the success achieved by a united pharmacological and chemical study.

And now the story is brought to the present day. I have omitted many lesser chapters, and I realize that many more chapters may still come to be written. I have found it a fascinating subject. To each student listening I would now make a simple request. When next you handle the ergometrine ampoule pause for a moment. Give a thought to the strange fungus that infests the head of the rye grass, to St. Anthony and his monks, to the immense sum of learning that ergot research has added to medical science; and, not least, thank God for His provision of this strange and wonderful medicine.

Much of the historical material contained in this paper is derived from G. Barger's *Ergot and Ergotism* (Gurney and Jackson, London, 1931) and from the original publications quoted in that work; also from *Religious Dances in the Christian Church and in Popular Medicine* (Allen and Unwin, London, 1952). Regarding the chemistry of ergot much help has been obtained from A. Stoll's numerous publications, notably *Recent Investigations on Ergot Alkaloids, Chem. Reviews*, 47: 197, 1950; also from the publications of A. L. Glenn (*Quart. Rev. Chem. Soc.*, 8: 192, 1954) and A. C. White (*Quart. J. Pharm. & Pharmacol.*, 16: 344, 1943; 17: 1 and 95, 1944). To the latter worker and to Professor J. H. Burn I am also indebted for helpful advice and references. The following is a brief list of special references.

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LEAD POISONING PROTECTION

A safety standard to protect children from lead poisoning, developed under the sponsorship of the American Academy of Pediatrics and approved by the American Standards Association, has been published and distributed in the U.S.A. The protective measure provides for limiting and labelling the lead content of paint used on surfaces—such as that of toys and furniture—which might be chewed by children.

This danger has increased with the development of the "do-it-yourself" movement because parents may use toxic paints on toys, furniture and interior surfaces.

The new standard, designated officially as "American Standard Specifications to Minimize Hazards to Children from Residual Materials, Z66.1-1955," specifies that the allowable lead content of such coatings as might be chewed and swallowed by children shall not exceed 1% of all solids, including pigment and drier. Use of toxic substances such as arsenic, antimony, barium, cadmium and mercury, in such coatings is excluded by the standard. The standard provides paint retailers and parents alike with a guide in the selection of special purpose paints safe to use on surfaces with which small children may have frequent contact.

The Lead Industries Association, the New York Paint, Varnish and Lacquer Association, and paint companies played a leading role in initiating the project and in the work of the Subcommittee on Residual Coating Materials, which is part of the over-all National Committee on Hazards to Children, headed by Dr. Wheatley, which was created in 1953 to set up "specifications, tests and procedures to minimize home hazards to children."

Canad. M. A. J.
May 15, 1955, vol. 72

GOUT*

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GOUT IS UNIQUE as a rheumatic disease for at least two reasons: first, because of the disturbed uric acid metabolism that is an integral part of the disorder, and second, because it is featured by acute attacks of arthritis which respond selectively to certain drugs ineffective in other types of arthritis.

The disturbance of uric acid metabolism is manifested by a raised uric acid level in the blood, increased stores in the tissues, and, in about 25% of cases, increased excretion in the urine. The gouty patient has a serum uric acid level usually in excess of 6 mgm. %, whereas the normal patient has one usually below 5 mgm. %. A level between 5 and 6 mgm. is shared by a few normal, usually plethoric individuals, and an occasional gouty patient. Serum uric acid levels in gout fluctuate a certain amount from time to time, but generally remain high.

This hyperuricæmia in gout reflects the increased stores of uric acid in the tissues. The size of the store in any patient can be measured by feeding uric acid containing heavy nitrogen in the first and third positions of the molecule, and measuring its rate of excretion in the urine. A normal person has about 1 gram of uric acid stored in his body, and from 50 to 75% of this is turned over each 24 hours. A gouty patient has usually two or three times this amount, and sometimes much more, but does not metabolize proportionately as much of his body stores each day.

When uric acid in tissue fluids reaches a certain concentration, it precipitates as yellowish deposits known as tophi. These deposits form in bones and joints, in bursæ, in cartilage and in certain internal organs, principally the kidney. The amount of uric acid contained in such deposits cannot be measured by techniques currently available.

The cause of this accumulation of uric acid in the body is not known. Nor is the reason for the acute attacks of arthritis which are such a characteristic clinical feature of the disease. The level of serum uric acid does not seem to be responsible. Rather, attacks seem to follow stress of one sort or another—a debauch, an operation, fatigue, unusual physical activity, or metabolic changes induced by one mechanism or another, including administration of certain drugs. It is, however, true that patients with large tissue stores of uric acid are more subject to acute attacks than those less seriously afflicted.

It is important to realize that most patients who have a gouty diathesis suffer no more than sporadic attacks of acute gout at rare intervals. Only a few patients develop a chronic deforming gouty arthritis.

The physician, therefore, has to deal most frequently with the problem of acute gout, and he has a choice of three drugs, each of which is likely to be effective in curing the acute attack. These are, in chronological order of their introduction into therapeutics: colchicine, ACTH and cortisone, and phenylbutazone.

COLCHICINE

Colchicine has been used for years to treat acute gout and its antiphlogistic action is so specific for this disease that response to colchicine has been used as a therapeutic test of the presence of gout. It brings about prompt clinical improvement followed by restoration of sedimentation rate and plasma fibrinogen to normal as depicted in Fig. 1. These laboratory tests are a measure of the acuteness of tissue inflammatory reaction, and improvement in the figures parallels, after a slight delay, the clinical response. Note that improvement does not come about overnight; almost two weeks elapsed in this case before colchicine could be discontinued with safety. The dose of colchicine tolerated by this patient was in excess of that tolerated by many. The specificity of action in gout is illustrated in Fig. 2, where two weeks of therapy with colchicine in a case of rheumatoid arthritis is shown to be without effect.

Colchicine is not, however, uniformly successful in gout. About 25% of any large series of cases will prove refractory in greater or lesser degree. To some extent, success depends upon promptness of administration. If an attack of gout gets well established, the amount of colchicine needed to control it may be large enough to produce gastrointestinal upset—cramps and diarrhœa, and less often nausea and vomiting—before it relieves joint pain. This toxic effect on

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Canad. M. A. J.
May 15, 1955, vol. 72

the gastrointestinal tract materially interferes with effective use of the drug. As little as 2 or 3 mgm. may bring on diarrhœa before joint pain has been relieved, making it impossible to continue treatment despite concurrent administration of opiate to splint the bowel.

One can forecast, to some extent, the patient's tolerance to the drug by his normal bowel habits. If bowels are costive, colchicine may act merely as a gentle laxative; but if they are irritable, it may prostrate him. It is wise practice not to prescribe more than 4 mgm. in divided doses every 24 hours, and where gastrointestinal upset is anticipated to use colchicine intravenously in a dose of 3 mgm., which is less likely to upset the bowel. The injection can be repeated if necessary. Side-effects from colchicine other than gastrointestinal are rare, but an occasional patient is hypersensitive, and a few fatalities have been reported after as little as 4.5 mgm. of the drug. Histological study in one fatal case revealed massive necrosis of the germinal centres of lymph nodes where the antimitotic action of the drug might be expected to exert its greatest effect.

An antiphlogistic action is the only demonstrable action of colchicine in gout. It has no effect on uric acid metabolism.

ACTH AND CORTISONE

In view of these limitations of colchicine it is fortunate that other agents are now available for use.

For those who are unresponsive to or intolerant of colchicine, ACTH or cortisone may be used. There is some evidence that ACTH is more effective than cortisone. It almost invariably terminates the acute attack in rapid fashion but there is danger of relapse after it is discontinued. In order to avoid this, ACTH should be continued for several days or combined with small doses of colchicine. Quickest relief can be obtained by giving 25 mgm. in an intravenous drip followed by 40 units of long-acting ACTH, given intramuscularly at gradually lengthening intervals. ACTH and cortisone apparently do not act by the same mechanism as colchicine for they may succeed where colchicine fails, and vice versa. Furthermore, their antiphlogistic action is not confined to gout but is common to most rheumatic diseases.

The action of ACTH in gout is not confined to relief of pain. It increases urinary excretion of uric acid and depresses the serum uric acid level, functions which have nothing to do with its anti-inflammatory action.

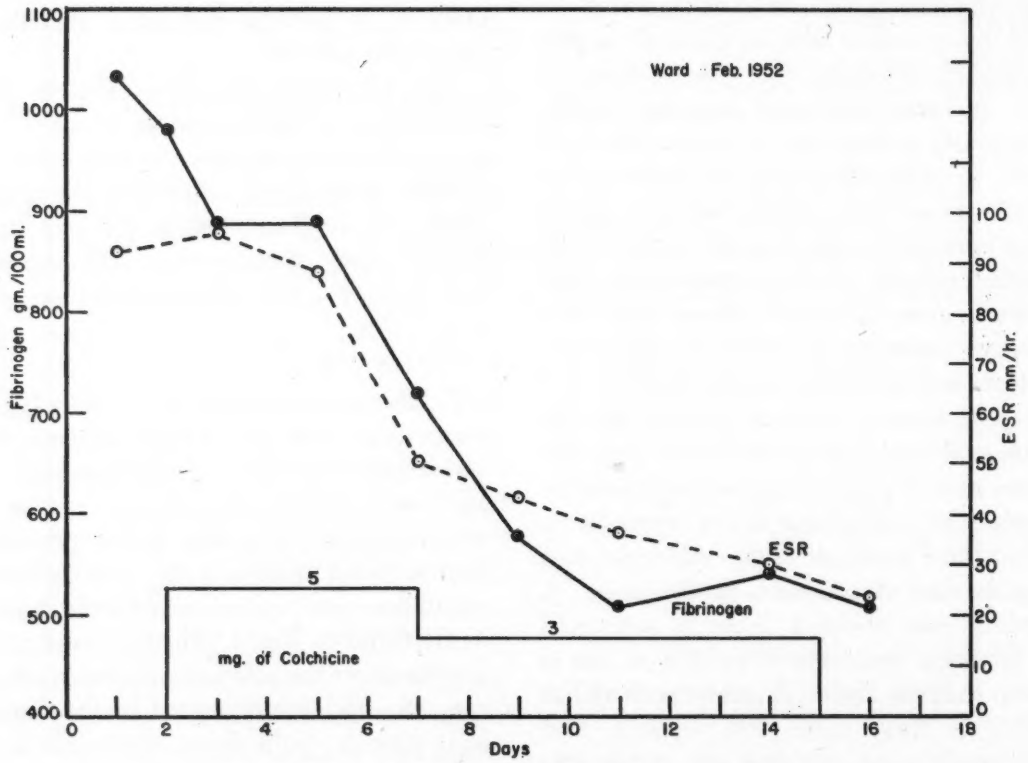

Fig. 1.—Effect of colchicine on ESR + fibrinogen in gout.

PHENYLBUTAZONE

Phenylbutazone is the third drug available to treat acute gout. It is the most successful anti-rheumatic agent to appear since ACTH and cortisone. Like colchicine it has a selectively antiphlogistic action in gout which is not reproducible in other rheumatic diseases. A daily dose of 0.5 to 1 gm. in divided doses provides prompt relief of symptoms—as prompt and as often as with colchicine—but without the danger of major gastrointestinal disturbance. This is a major point in its favour. Phenylbutazone is also available as a 20% solution for intramuscular injection when the quickest possible effect is desired. The dose should be reduced gradually as clinical improvement takes place. Small amounts of the drug are well tolerated, but when it is given for weeks or months there is a high incidence of toxic effects, some of which have been serious and fatal.

Like ACTH and unlike colchicine, phenylbutazone increases uric acid excretion by the kidney and sharply depresses serum uric acid levels (Fig. 3).

In summary: acute gout can be terminated quickly by intravenous colchicine or ACTH, or intramuscular phenylbutazone. Danger of relapse can be avoided by subsequent oral administration of colchicine, cortisone, or phenylbutazone or intramuscular long-acting ACTH.

CHRONIC TOPHACEOUS GOUT

When a patient suffers from frequently recurring attacks of acute gout, and as time goes on begins to display tophi or develop chronic deforming arthritis, additional measures must be adopted to arrest the course of the disease and lessen disability. Some are of the opinion that colchicine has a use, not only to treat acute gout, but also to prevent recurring attacks. A daily dose of 1-2 mgm. is worthy of trial in those subject to frequently recurring attacks. Such a dose can be continued for months or even years without significant danger of toxicity.

Phenylbutazone also reduces the frequency of attacks but is too toxic to be recommended for this sort of therapy.

A more profitable approach to the problem of recurring attacks would be to correct the meta-

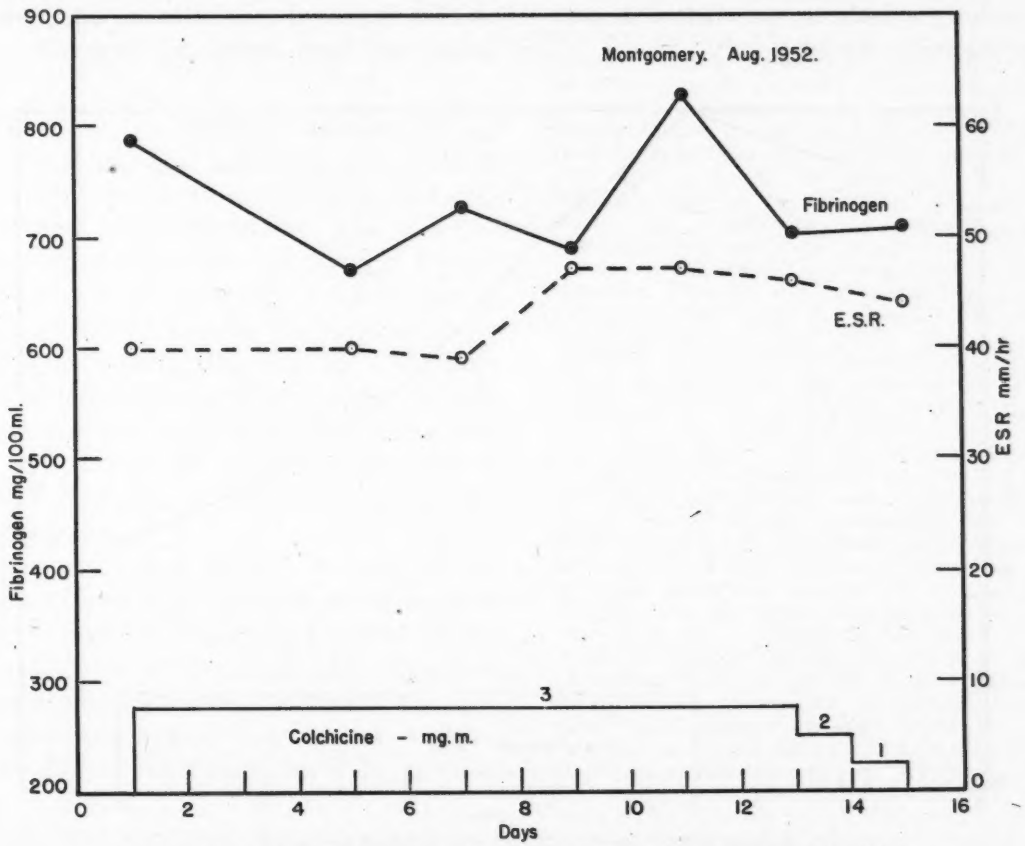

Fig. 2.—Lack of colchicine effect on ESR + fibrinogen in rheumatoid arthritis.

Canad. M. A. J.
May 15, 1955, vol. 72

bolic fault in urate metabolism, but unfortunately the physician is only able to toy with the fringe of the problem by attempting to limit formation of uric acid or by increasing its elimination by the kidney. So far measures which increase urinary excretion of uric acid hold more promise than those which limit its formation. Three drugs have been used for this purpose: salicylates, cinchophen and probenicid. I mention cinchophen only to discard it. It is analgesic and uricosuric but too toxic for continued use. It does nothing which is not better accomplished by the other two.

appeared in 2 cases; and ulcerations healed in 3 out of 4. These good results extended for periods of several months to over a year in 14 patients. Such results are gratifying but leave those of us who have tried to stuff large doses of acetylsalicylic acid into our patients wondering at his powers of persuasion. It has been this difficulty which has led to the recent adoption of another agent known as probenicid to serve the same purpose. Like acetylsalicylic acid, probenicid blocks tubular absorption of uric acid so that increased quantities are eliminated in the urine, and body stores are depleted.

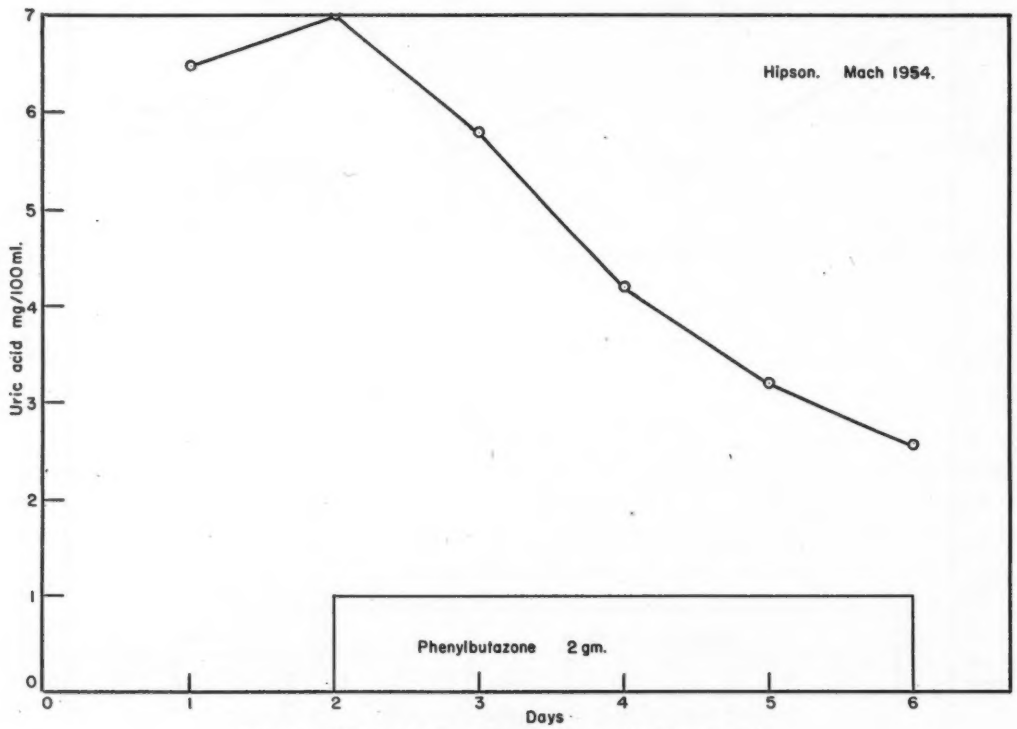

Fig. 3.—Effect of phenylbutazone on blood uric acid.

SALICYLATE

Salicylate has been used for a much longer period than probenicid. It sharply increases uric acid excretion by acting on the renal tubules to prevent absorption of uric acid which has filtered through the glomerulus, and in consequence lowers serum levels and body stores of uric acid. However, doses exceeding 4 gm. a day are necessary to produce this effect, and the belief has been held, rightly or wrongly, that effects wear off after a few months. Recently Marson has challenged this view. Using sodium salicylate in doses of from 4-9 gm. daily, he was able to reduce uric acid levels to normal and keep them there in 28 patients. Patients got relief from acute attacks of gout; tophi dis-

Unfortunately when acetylsalicylic acid and probenicid are given together, the combined effect is less than when either drug is given alone and may in fact be negligible. This means that if a patient is to use probenicid he must get along without the analgesic effects of acetylsalicylic acid.

The average daily dose of probenicid is 1-2 gm. in divided doses. Many patients have been carried on this dose for years with beneficial results. Both Gutman and Talbott report a decrease in the frequency of attacks, and Talbott has noted slight shrinkage of tophi in a few instances. Not only the clinical but also the metabolic effects of probenicid continue indefinitely.

No significant toxic effects have developed

despite long-term administration. Some nausea may develop, but this can usually be prevented by taking the drug with meals.

In summary, probenicid will reduce the frequency of attacks of acute gout, presumably through its ability to deplete body stores of uric acid. Acetylsalicylic acid will do the same thing in the same way, but the amount of drug necessary to bring this about is often not tolerated by the patient. Colchicine is also worthy of trial despite its inability to influence uric acid metabolism.

DIET

The other way of attacking the problem of chronic gout is to try to reduce the formation of uric acid. This has both endogenous and exogenous sources. The endogenous source is cell nucleoprotein, and the extruded nuclei of normoblasts are said to be particularly rich sources of uric acid. This may explain the increased incidence of gout in polycythæmia. The exogenous sources are varied. We now know that the body can synthesize uric acid from elementary substances, and this means that not only purines but also carbohydrates, proteins and fats are potential precursors.

Nothing can be done to alter the endogenous production of uric acid, and it is quite apparent from these recent findings that no rigid restriction of exogenous sources is possible. But there are patients whose urinary excretion of uric acid can be modified a good deal by diet, and undoubtedly dietary restriction should be given its chance.

Gutman's plan is to prescribe at first a Spartan diet which eliminates purines, restricts proteins and fats, and leaves the bulk of the food composed of cereals, grain products, eggs, cheese and milk, non-leguminous vegetables and fruits. After a while he loosens restrictions and watches developments. Patients, by their own choosing, continue to curb their appetites. Even where no strict diet is followed, it is wise to avoid gluttony and debauch because as stresses they may provoke acute gout.

CONCLUSION

In conclusion, it is possible to say that acute gout can now be controlled with ease and dispatch by several remedies presently available, and that a measure of success has been obtained in modifying the natural course of chronic gout. In this, as in other rheumatic disorders, advances during the past five years, after so many decades of inertia, justify a feeling of optimism and hope for the future.

RÉSUMÉ

Les troubles du métabolisme de l'acide urique ainsi que l'effet thérapeutique d'agents bien spécifiques caractérisent la goutte et la différencient des autres formes de rhumatisme. Le taux de l'acide urique du sérum est habituellement de 6 mg. % ou plus chez les goutteux. Un podagre peut atteindre une hyperuricémie de 2 ou 3 grammes (normale: 1 Gm.). Au-delà d'une certaine concentration, l'acide urique se précipite en dépôts jaunâtres appelés tophi. Les manifestations aiguës d'arthrite semblent suivre les périodes de fatigue, quelle qu'en soit la cause; activité physique, intervention chirurgicale, excès de table, voire même l'administration de certains médicaments. Les goutteux, pour la plupart, ne sont sujets qu'à des attaques aiguës, mais isolées. Rares sont ceux chez qui la maladie devient chronique. Le colchique est le remède le plus ancien dans le traitement de la goutte; c'est aussi un spécifique, bien que 25% environ des cas répondent peu ou pas, probablement parce qu'il n'est pas administré d'emblée. Dans les cas où la diarrhée risque de faire échouer le traitement, la colchicine intraveineuse peut être employée à raison de 3 mgm. par 24 heures. L'ACTH et la cortisone peuvent faire avorter une attaque en peu de temps, mais on doit en continuer l'administration pendant plusieurs jours, de préférence avec de petites doses de colchicine. Le phénylbutazone est la médication la plus récente dans le traitement de la goutte. On l'administre en doses de 0.5 à 1 gramme par jour. L'administration prolongée peut donner lieu à des effets toxiques quelquefois très graves. Les malades sujets à des attaques fréquentes peuvent recevoir 1 ou 2 mgm. par jour de colchicine pendant des mois ou même des années. On a aussi recommandé l'emploi dans les mêmes circonstances de salicylate de cincophène et de probénicide (benemid). Le salicylate à hautes doses (4 grammes par jour et plus) permet l'excrétion d'acide urique. Le probénicide parvient à un effet semblable mais par un mécanisme différent (la dose: 1 à 2 grammes par jour). Le régime à suivre dans la goutte cherche à diminuer la formation d'acide urique en éliminant les aliments qui peuvent y contribuer. Si l'on se rappelle que non seulement les purines mais aussi les hydrates de carbone, les protides et les glucides peuvent également contribuer à la synthèse de l'acide urique, on se rend compte de la difficulté qu'il y a à choisir un régime satisfaisant. Il semble cependant qu'une abstinence modérée, quels que soient les aliments sur lesquels elle porte, aide à juguler la maladie.
M.R.D.

TETRACYCLINE IN SONNE DYSENTERY

In a small comparative trial of tetracycline, sulphathiazole and oral streptomycin in the treatment of Sonne dysentery, tetracycline was successful in 26 of 27 cases, phthalyl sulphathiazole in only 11 of 32, and streptomycin in nine of 25. The dosage of tetracycline was 500 mgm. six hourly for seven days in persons over 15, with 250 mgm. doses at 5-15, and 125 mgm. doses in younger children. Success was judged by finding of six consecutive negative stools at the end of therapy.—Abbott, J. D. and Parry, H. E.: *Lancet*, 1: 16, 1955.

Canad. M. A. J.
May 15, 1955, vol. 72

MORTALITY IN CONGENITAL CARDIOVASCULAR SURGERY*

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THE RECORDS at the Hospital for Sick Children show congenital heart disease as the leading cause of death in all age groups. In order to reduce this mortality more of these patients must be operated upon and for that reason we felt it wise to review our experience and to report our statistics on mortality following surgery.

Over the past few years there has been a trend toward life-saving procedures in infancy, with a resulting high mortality. We have never turned down a case because of poor surgical risk and have operated upon many moribund patients. Statistics from other clinics are often based more or less upon selected groups and do not really show mortality in its true light. For example, if one did not operate upon tetralogy of Fallot before three years of age the mortality figures would be much better for the surgeon but not for the patients, since a number would be dead before operation was undertaken. We feel that in the infant any operative mortality which is less than 100% is certainly justifiable, since only those infants who would not live past their second or third year would be operated upon.

In this analysis we included all our cases up to June 1954, to give a complete picture of the mortality and the various operable lesions. Over the course of years more and more congenital defects will become operable, and as the list grows the mortality figures may not change significantly. A study of Fig. 1 will show that we have made reasonable progress in dealing with five out of eight congenital abnormalities.

Patent ductus arteriosus.—Fig. 2 demonstrates clearly that our efforts in the age group under two when operation is undertaken as a life-saving measure have been very successful.[1] These cases constitute the so-called morbid ductus group in which the infant's heart is enlarging or the infant is in heart failure. The two deaths, one

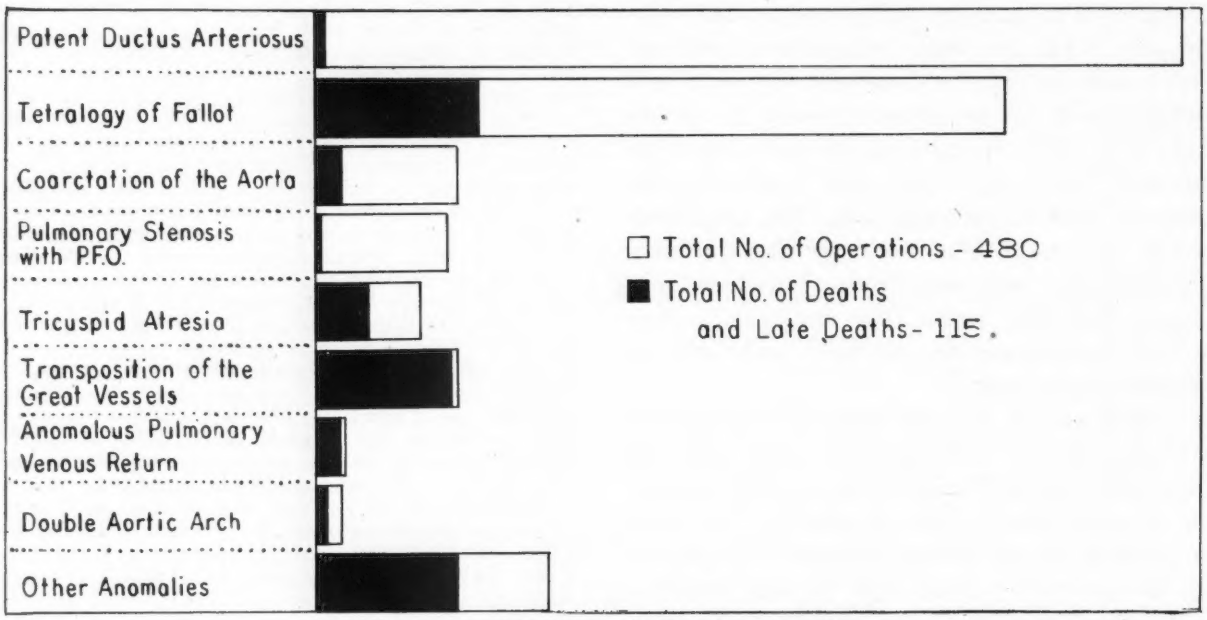

Fig. 1.—Summarizing table of all cardiac operations.

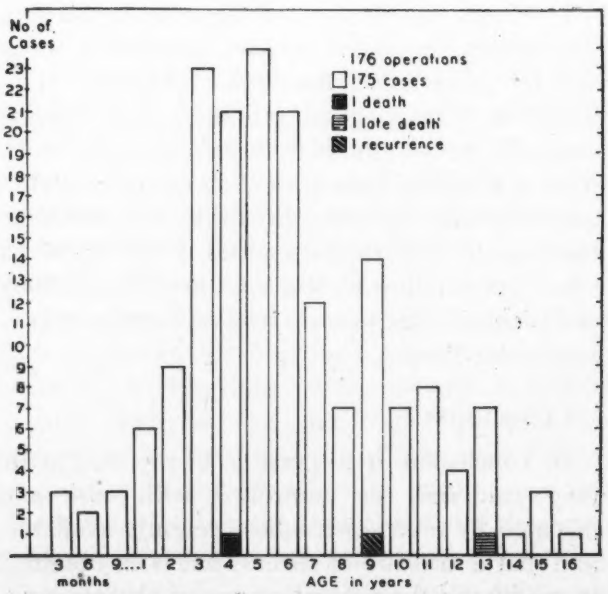

Fig. 2.—Patent ductus arteriosus: uncomplicated cases.

*From the Department of Surgery, Hospital for Sick Children, Toronto.

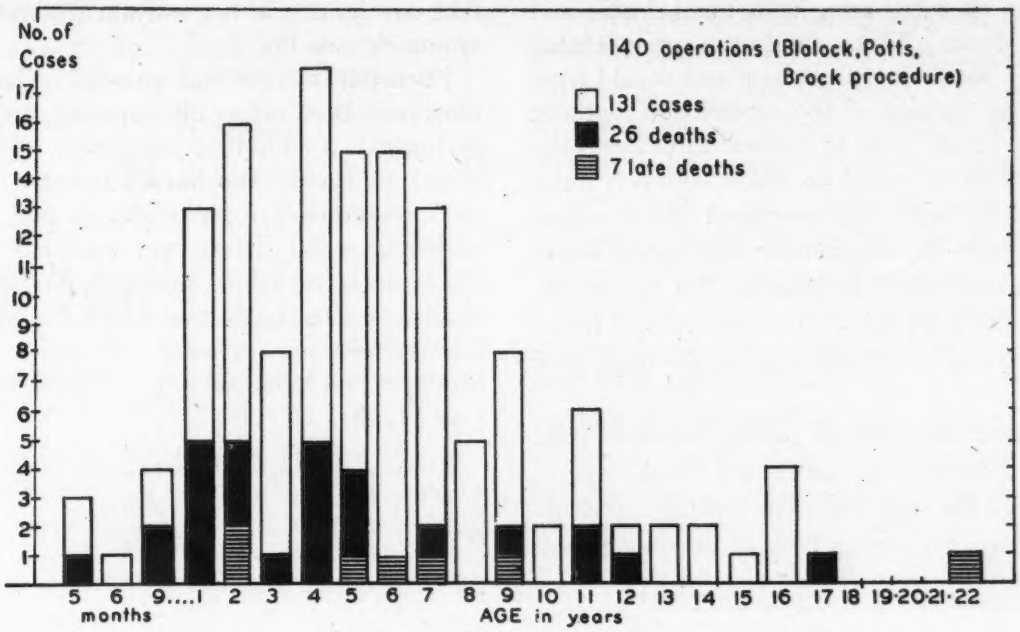

Fig. 3.—Tetralogy of Fallot.

early and one late, in this group are in cases in which the ductus flow was reversed and pulmonary hypertension was present. Postoperative recovery is prompt and there are very few complications.

Tetralogy of Fallot.—Under the age of two, operation is undertaken as a life-saving measure and one is faced with a high mortality. However, if one considers that these patients would have died if left to an elective age of three or four, the figures are encouraging. We have employed the shunting operations rather than direct attack, and feel that the direct attack should be left until not only can the infundibular stenosis and pulmonic stenosis be corrected but also the intraventricular septal defect closed. If the anastomosis is successful, all cases are improved. What the ultimate fate of the patients will be is a matter for conjecture at present. Occasionally the anastomosis may be too large, or simply the presence of the anastomosis itself may cause heart failure. However, we feel that this is a calculated risk and the advantages far outweigh the disadvantages of no operation (see Fig. 3).

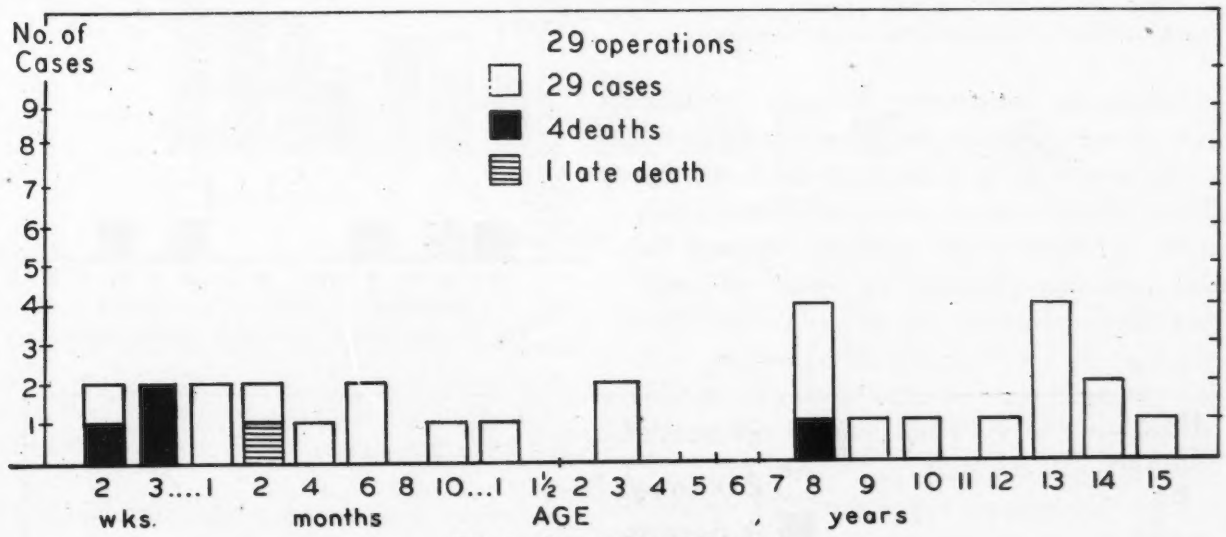

Fig. 4.—Coarctation of the aorta.

Coarctation of the aorta.—As a result of the efforts of John Keith and associates in cardiology, our attention has been directed toward life-saving operations in infancy. Thirteen infants

Canad. M. A. J.
May 15, 1955, vol. 72

have been operated upon with three deaths and one late death.[2] These children were operated upon as a life-saving procedure and would have died, in the opinion of the cardiologist, without operation. If one were to exclude these cases the mortality figures would be much better. A number of these early cases represent the so-called infantile type of coarctation which previously has been considered inoperable. On the whole, the results of resection of the coarcted and hypoplastic segment have been most encouraging (see Fig. 4).

Pulmonary stenosis with patent foramen ovale.—We have consistently performed Brock's operation through the right ventricle, cutting and dilating the valve. We prefer Potts's instruments, and

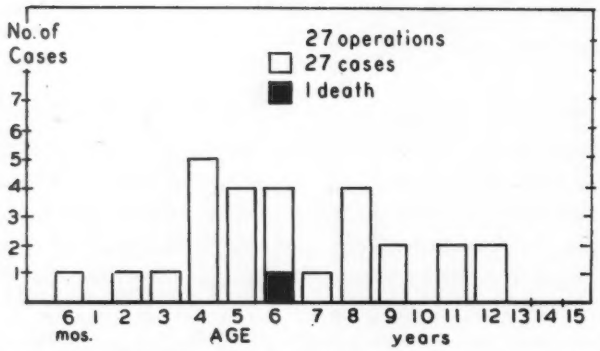

Fig. 5.—Pulmonary stenosis with patent foramen ovale.

our results are satisfactory. However, although many of our cases have not shown a marked fall in right ventricular pressure, it is safe to say that all have been improved by the procedure, which carries a relatively low mortality. Perhaps the open operation proposed by Swan[3] will supplant blind operations, but as yet we have felt that our results do not warrant the more radical approach (see Fig. 5).

Tricuspid atresia and stenosis.—These conditions have been rather discouraging, and we have performed a shunting operation (Blalock or Potts) routinely. We have attempted to create an interventricular septal defect and an intra-auricular septal defect and combine this with the Blalock procedure, anastomosing the innominate artery to the pulmonary on the right. With this combined approach, mortality may be lessened and clinical improvement be greater (see Fig. 6).

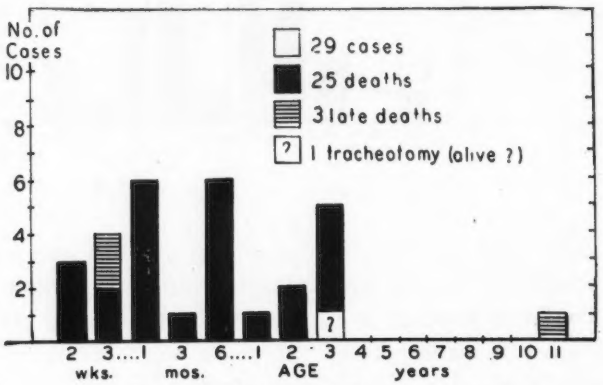

Fig. 7.—Transposition of the great vessels.

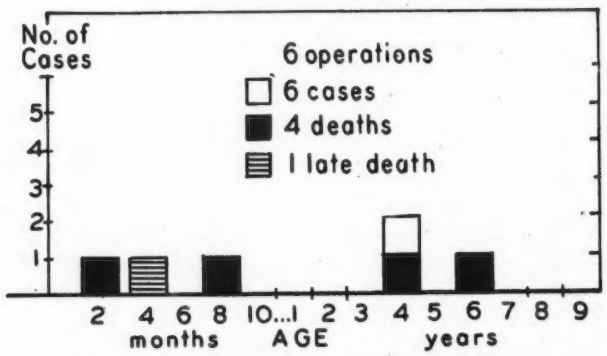

Fig. 8.—Anomalous pulmonary venous return.

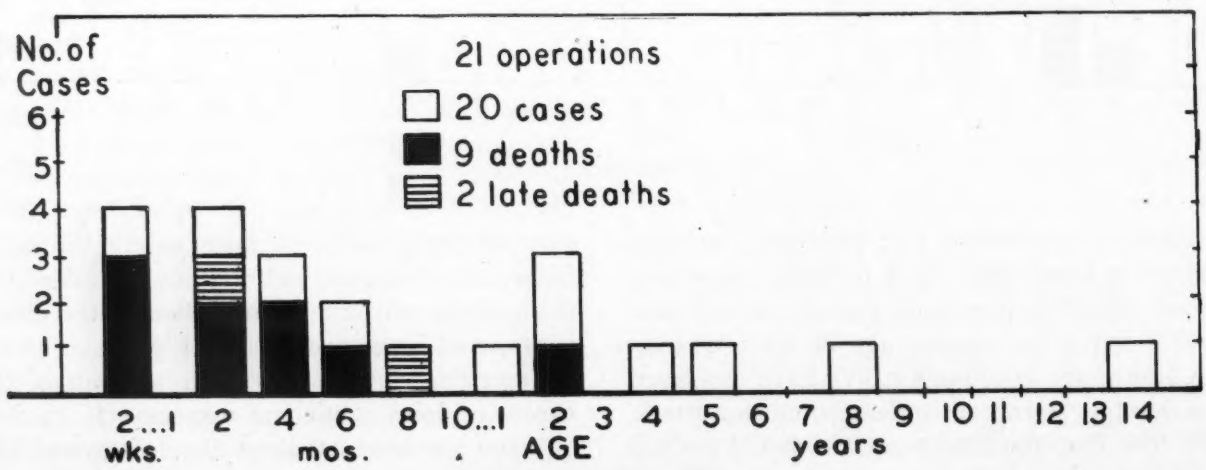

Fig. 6.—Tricuspid atresia.

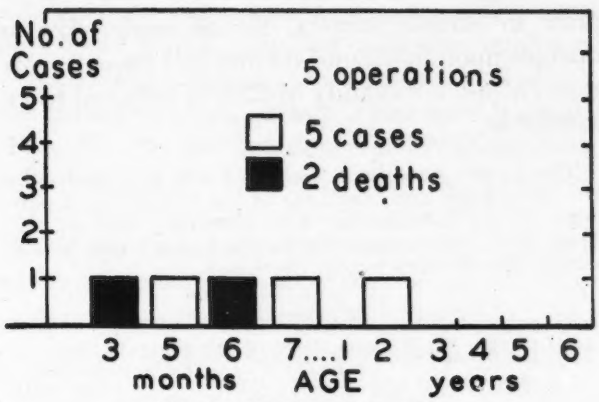

Fig. 9.—Double aortic arch.

Transposition of the great vessels.—This anomaly is a real challenge and we have not yet accomplished the operation successfully.[4] Not only is it a question of transposing the great vessels, but one or more of the coronary vessels must also be transposed. We feel reasonably certain that this will be accomplished in the very near future with the use of an extracorporeal circuit (see Fig. 7).

Total anomalous pulmonary venous return (into the left innominate vein).—Results in these cases have been most encouraging. We have now had two more successful cases at the time of writing, and we believe that hypothermia has been responsible for the success in these cases.[5] There will always be an operative mortality, but we feel that with the further perfection in technique this could be reduced considerably. It is our belief that these patients can be cured surgically (see Fig. 8).

Double aortic arch.—We were somewhat surprised to find that we had so few cases and that our results were not spectacular. Following the operation one would expect these children to do very well, but certainly our two deaths which occurred a few days after operation have depressed us somewhat. It may be true that the operation for double aortic arch should be postponed until later in life, at which time it might become evident that operation is not necessary in most cases (see Fig. 9).

Other anomalies.—The other anomalous group comprises a mixture of varied congenital defects that may never be amenable to surgery (see Fig. 10).

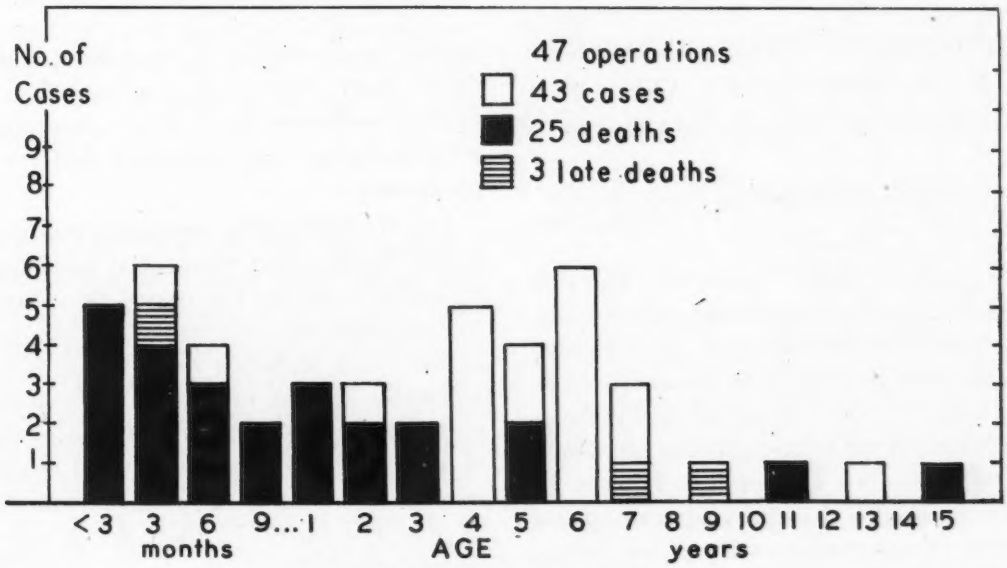

Fig. 10.—Other anomalies.

SUMMARY

The purpose of this paper is to acquaint the medical profession with our experience in congenital heart surgery and the risk involved. Dr. John Keith and his associates who have been responsible for these cases through the cardiac clinic at the Hospital support the belief that the child who is in heart failure or dying as a result of his heart disease should have surgery offered: there is a hope of salvaging a group of these children.

During the past year we have given hypothermia, introduced by Bigelow, an extensive trial.[6] The cyanotic child becomes less cyanotic as the temperature is lowered and the danger of interruption of pulmonary circulation consid-

Canad. M. A. J.
May 15, 1955, vol. 72

erably lessened. We feel that some degree of hypothermia should be employed routinely in the cyanotic case. A temperature of 25° C. has enabled us to complete an anastomosis of the anomalous venous trunk to the left auricle in three cases of complete anomalous pulmonary return. We allowed the heart to stop completely for periods of 3-6 minutes to complete the anastomosis.[5]

Mortality figures must be presented honestly and include all cases operated upon, and the deaths which are not necessarily due to operation must be shown as such, since a ready comparison exists in these congenital abnormalities prior to cardiac surgery. If one undertakes to operate upon moribund infants and those in cardiac failure, a mortality of 25% is believed to be justifiable.

These cases have been diagnosed and investigated by Dr. John Keith and associates at the cardiology department of the Hospital for Sick Children, Toronto. Dr. Anna Sirek was responsible for the tedious task of collecting the statistics herein presented.

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EXPOSURE TO VIRUS DISEASES IN EARLY PREGNANCY AND CONGENITAL MALFORMATIONS

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SINCE 1941, when Gregg[1] reported harmful effects of maternal rubella upon the fetus, many series of pregnancies complicated by this and other virus diseases have been studied. The findings, which have been well summarized by Kaye, Rosner and Stein,[2] point to an excessive incidence of congenital anomalies among infants born to mothers who suffered a virus infection during the first trimester of pregnancy, the excess being most marked when the infection was German measles but suggestive also in the case of such other diseases as mumps, measles and chickenpox.

Since the likelihood of frank maternal infection with German measles and other virus diseases is not great, one would hardly expect that the total incidence of congenital malformations would be greatly affected by this specific hazard. Schick,[3] however, has raised the interesting question as to whether a mother immune to a virus disease herself might not still be capable of infecting the fetus if she were exposed to the disease and acquired some degree of subclinical infection.

With these thoughts, and particularly the latter, in mind it seemed worth while to determine whether there is any relationship between the annual and seasonal fluctuations in infant mortality from congenital malformations and the general incidence level of the common viral infections in the corresponding first trimesters of pregnancy.

(a) *Mortality from congenital malformations.*—Infant deaths from congenital malformations by calendar month for the period from January 1944 to July 1951 were obtained for Canada from the annual vital statistics reports published by the Dominion Bureau of Statistics. From these, mortality rates were computed expressing the number of infant deaths from congenital malformations in a given month as a proportion of the average of the live births in that month and the preceding month.*

(b) *Incidence of virus diseases.*—For each of six virus diseases a measure of the general incidence in the Canadian population was obtained for each calendar month from June 1943 to December 1950 in terms of the notified cases of the disease per million mid-year population at all ages. The virus diseases studied were: German measles, measles, mumps, chickenpox, poliomyelitis, and epidemic influenza.

(c) *Relating the infant mortality from congenital malformations to the exposure to virus diseases in the first trimester of pregnancy.*—The monthly rates of infant mortality from congenital malfor-

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*It is a well-known fact that most of the infant deaths from congenital malformations occur soon after birth. In Canada in recent years the proportion of such infant deaths occurring between birth and the end of the second month of life has been consistently between 72 and 74%. Therefore, it is reasonable to use the average of the births in the month of death and the preceding month as a denominator for the congenital-malformation death rate.

mations from January 1944 to July 1951 were plotted on graphs, together with the incidence of each virus disease during the corresponding first trimesters of pregnancy. Thus in each graph (Figs. 1 to 6) the first congenital malformation death rate is for January 1944, and plotted directly beneath this is the case rate of the virus disease for June 1943. The month of June 1943 would correspond to some part of the first trimester of pregnancy for the majority of the mothers of infants dying from congenital malformations in January 1944.* By this method a rough approximation can be made of the relation between maternal exposure to virus diseases in the early months of pregnancy and the mortality from congenital malformations among infants born to those mothers. From an actuarial point of view this method leaves something to be desired, but in the absence of the data necessary for more refined techniques it was accepted as being sufficiently accurate to reveal any outstanding relationships.

RESULTS

Figs. 1 to 6 illustrate the results of this analysis. Looking first at the death rate from congenital malformations, which is plotted as a solid line in each graph, it is apparent that over the period studied there were considerable fluctuations. The rates ranged from a low of 4.3 to a high of 7.9 per 1,000 live births. A fairly consistent seasonal trend is evident, the higher rates occurring from November to March and the lower rates from June to September. Although no clear-cut trend in the year-to-year fluctuations can be recognized, there is some indication of an over-all decline. The highest annual average rates were in 1945 and 1946, and the lowest in 1950 and 1951.

Turning to the comparison of the congenital malformation death rates with the incidence of the virus diseases, it can fairly be said that no striking relationship emerges from any of the six comparisons. Although sometimes the seasonal peaks in the death rate seem to be associated with corresponding rises in the incidence of viral diseases, this tendency is by no means consistent and for chickenpox is not apparent at all. One might argue, with reason, that a true seasonal correspondence could have been obscured by plotting disease incidence for single months only, since, by definition, the first trimester of pregnancy is of three months' duration. Analyses were made by employing three-month moving averages of the incidence of each virus disease, and the results (which for the sake of simplicity are not shown) did not yield any stronger evidence of a seasonal association.

More important than the question of seasonal coincidence is that of the year-to-year relationship. In this sense, it is quite apparent from the

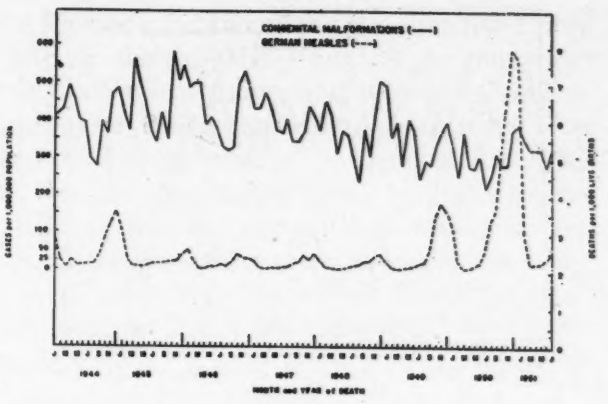

Fig. 1

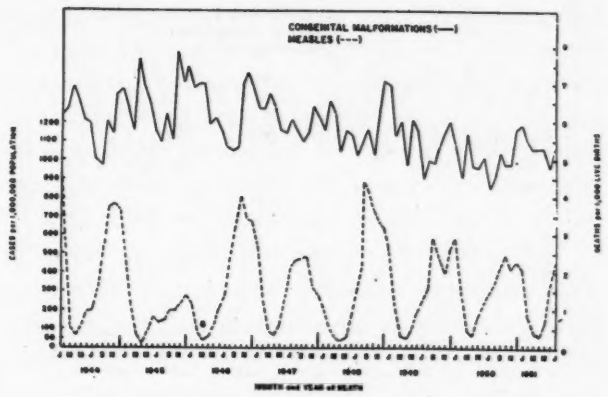

Fig. 2

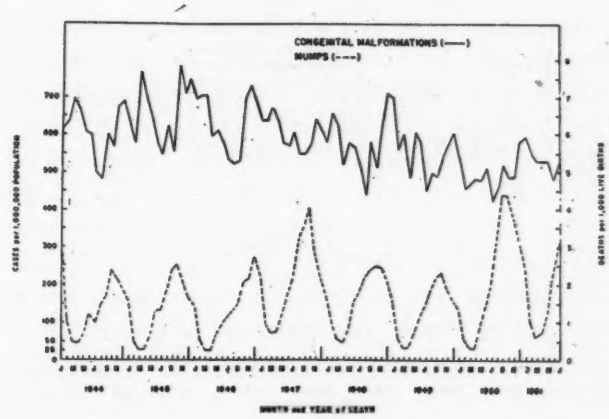

Fig. 3

*As already stated, the majority of infants dying from congenital malformations in January 1944 will have been born in that month or in December 1943. The month of June 1943 represents the second to third month of pregnancy for births in January 1944, the third to fourth month of pregnancy for births in December 1943, and the first to second month of pregnancy for 8-month premature infants born and dying in January 1944.

Canad. M. A. J.
May 15, 1955, vol. 72

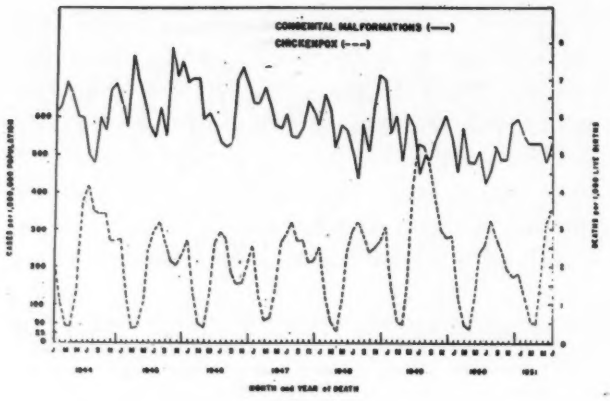

Fig. 4

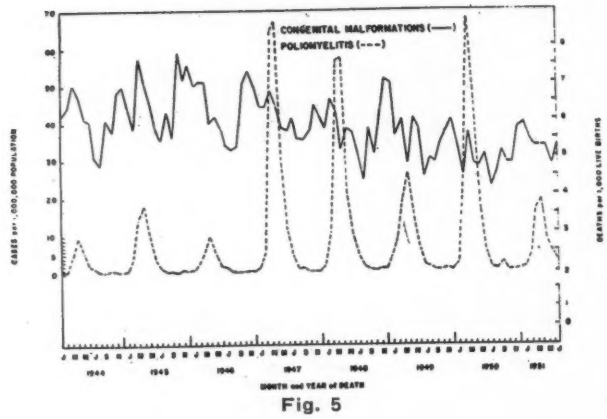

Fig. 5

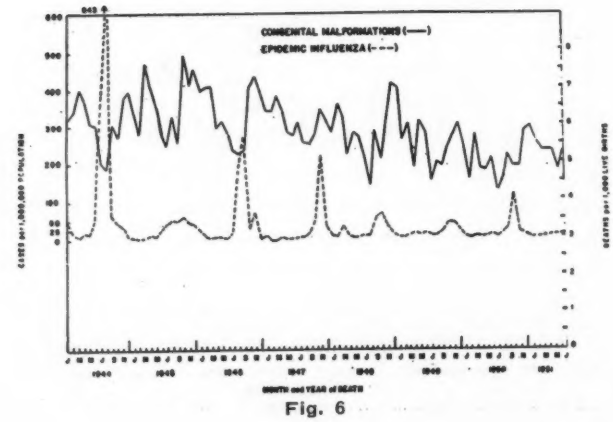

Fig. 6

graphs that the level of incidence of the different diseases has little association with the magnitude of the death rate from congenital malformations. Variations in incidence were considerable, with rises of epidemic proportions in the rates for German measles, influenza and poliomyelitis. However, for none of the six diseases does the highest incidence coincide with the highest rates of mortality from congenital defects.

DISCUSSION

If variations in exposure to a virus disease in early pregnancy were an important factor in producing the fluctuations in the infant death rate from congenital malformations, it should be apparent from an analysis such as this. One would expect to find both seasonal and year-to-year associations between the two events. Such associations, and particularly the latter, were not found for the period and the diseases studied. Therefore, one is led to conclude that, although in the individual case a virus infection early in pregnancy may give rise to congenital malformation of the infant, this fact does not explain the observed variations in the infant death rate from congenital defects. Whether an analysis covering a longer period of time, or including other virus diseases, would alter this conclusion is of course open to question. However, it seems likely that we must seek elsewhere for the causes of the interesting fluctuations in this particularly important area of infant mortality.

SUMMARY

The infant death rate in Canada from congenital malformations has been found to fluctuate seasonally and from year to year over the period from January 1944 to July 1951. There is no convincing evidence that these fluctuations are associated with variations in maternal exposure to German measles, measles, mumps, chickenpox, influenza or poliomyelitis in the first trimester of pregnancy.

The writer is grateful to Mr. H. G. Page and Dr. R. Kohn of the Dominion Bureau of Statistics for the provision of data on communicable diseases in Canada.

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RÉSUMÉ

On s'est rendu compte depuis 1941 qu'une infection à virus pouvait, dans les premiers trois mois de la grossesse, être la cause d'anomalies congénitales. Schick s'est même posé la question de savoir si une mère possédant elle-même de l'immunité ne peut pas résister à un virus qui pourrait infecter le fœtus. Il semble que le taux le plus élevé de mortalité des nouveau-nés ait lieu de novembre à mars de chaque année, tandis que la période de juin à septembre correspond à une baisse dans cette mortalité. Il n'existe aucune corrélation évidente entre ces données et la fréquence annuelle des maladies contagieuses à virus. L'auteur conclut que les maladies à virus sont responsables pour un petit nombre de malformations congénitales, mais qu'elles n'expliquent pas la majorité de la mortalité infantile causée par ces malformations. M.R.D.

Canad. M. A. J.
May 15, 1955, vol. 72

SEGMENTAL RESECTION IN PULMONARY TUBERCULOSIS*

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SEGMENTAL RESECTION is now an accepted surgical procedure in the treatment of pulmonary tuberculosis. We should like to describe briefly our experience with this operation during a two-year period extending from April 1, 1952 to April 1, 1954. During this time we had the opportunity, at Laval Hospital, Quebec, and at Quebec Veterans Hospital, to perform some 45 segmental resections. These we have divided into two main groups: Group 1: Those cases in which a complete upper lobe was removed, plus the apical segment of the lower lobe. There were 11 such cases, and they are not included in this presentation. Group 2: The remaining 34 cases. They were all what one could call "straight segmentals," consisting of the removal of one or more segments of an upper lobe. This was usually done by anatomical dissection, but occasionally by a simple wedge excision. These are the cases we should like to discuss.

When we began performing resections for pulmonary tuberculosis in the fall of 1951, we were, shall we say, afraid of segmental resections. Our cases for surgery were presented at the medical-surgical conference, and at that time it was always decided that excisional therapy should consist either of a pneumonectomy or a lobectomy. Like all younger assistants, we respected this decision. So much so that when we published our first 50 cases of resection in 1952[1] only two cases (4%) were segmental. This percentage increased to 36% over the next 25 cases, and has remained at around that figure.

Why has our percentage of segmental resections increased so? First of all, we became very quickly convinced in the course of our lobectomies that often we were removing normal lung tissue. As a result we had some diminution in pulmonary function, and were often left with a large residual space calling for emphysematous changes, or a thoracoplasty with further reduction of pulmonary function, or complications such as broncho-pleural fistulæ or empyemas or both.

When we looked seriously into the question we realized—and I think this is an important principle in the surgical treatment of pulmonary tuberculosis—that, instead of helping and following nature, we are going against it. Medlar[2] had very well demonstrated the segmental situation of localized foci in the lobes. In demonstrating this, he had also naturally shown how infrequently some of these segments are affected. Fig. 1 is an anterior-posterior view illustrating Medlar's findings. Fig. 2 is a right lateral view of the same findings. Fig. 3 gives a left lateral view. Most of the foci are situated at the apex.

If we now transpose this over a segmental anatomically marked slide (Fig. 4), we see that the apical and posterior segments of the upper lobe are the most frequently diseased. Next come the apical segments of the lower lobe, and the other segments very infrequently. In Fig. 5 the freedom from infection of the anterior segments is well seen in the lateral view. In Fig. 6 the anatomical distribution is characteristic.

However, all this is schematic and too easy. The tuberculosis process does lie where we have indicated, but its location in space varies with time and treatment. By the time the patient comes to operation, good treatment and nature have worked out a healing process. The cavity may still lie in the apical posterior segment of the upper lobe, but it usually has become adherent to the parietal pleura, has shrunk down considerably, and has become atelectatic. During this time the rest of the lung has developed compensatory emphysema. If, for instance, the focus is in the apical and posterior segment, the anterior segment will have rotated upward and backward until it practically meets the apical segment of the lower lobe which has risen to meet it. This is an effort to shut off the diseased area lying between. Chamberlain[3, 4] described this very well and called it the segmental clock (see Fig. 7).

Lateral tomography has been a great help in locating lesions and in planning our surgery.

But we have come to feel that sometimes a whole lobe may be as atelectatic as a segment, with the same compensatory enlargement of the other lobes, and sometimes the planned segmental resection became a lobectomy. This has gradually modified our way of thinking, and we like to express ourselves now by speaking of "lesionectomies." Like all terms used in describing tuberculous lesions, I am sure there is much wrong with it, but it expresses our view.

*Presented at the annual meeting of the Canadian Tuberculosis Association, held in Saint John, New Brunswick, June 22-26, 1954.

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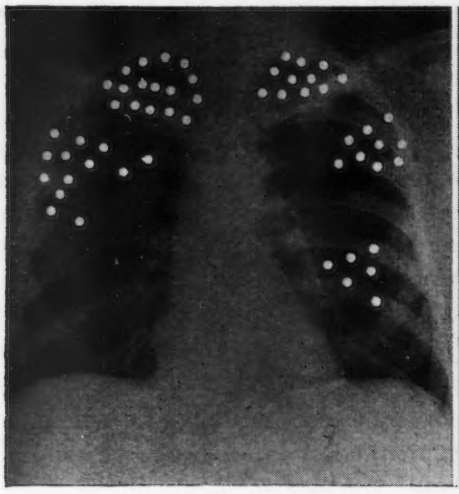


Fig. 1

Fig. 2

Fig. 3

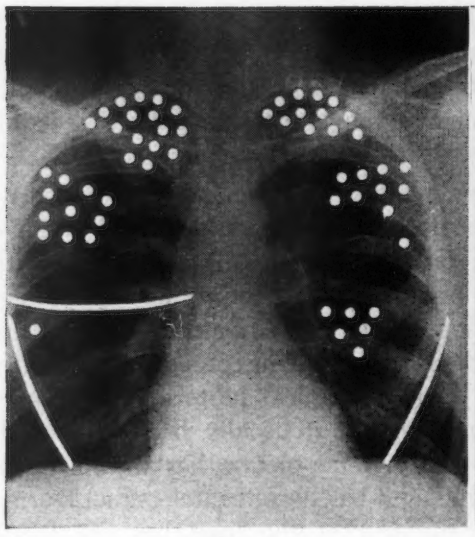
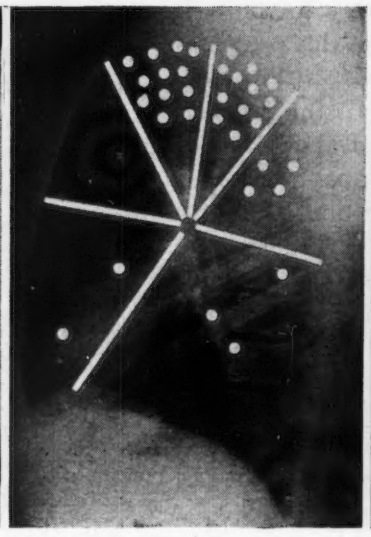


Fig. 4



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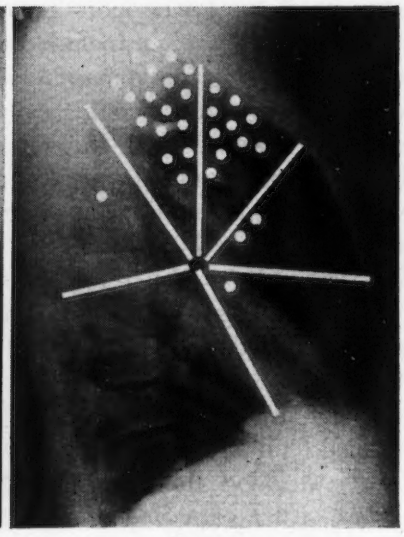


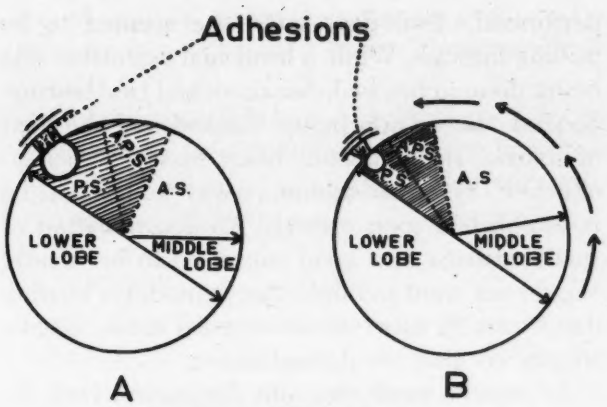
Fig. 6

Very often our cases are now accepted at the medico-surgical conference for an elective resection. This gives the operating surgeon enough leeway to do as he sees fit. We believe that no other means will give as accurate information as the visualization and careful palpation of the diseased lung. In such assessment we have found the following points of great help: (1) The careful opening of the pleural space in order not to disturb the existing picture. (2) The use of a Carlens tube which will permit complete control of each lung individually, and a dry tracheo-bronchial tree in spite of our manipulations. (3) A good preoperative knowledge of the pathology and its possible odd variants, based on good lateral laminography.

THE SELECTION OF CASES

As mentioned previously, early in our experience a segmental resection was seldom asked for and seldom performed. However, with time we realized that segmental resection could be done quite easily, and as a matter of fact seemed indicated in a rather large number of cases. But let us say, first of all, that one must not ask of this operation more than it can give. Trouble will come, says Chamberlain, if the indications for segmental resections are extended. By definition, a segmental resection removes one or more segments. If a cavity is ignored and left behind in a remaining segment, this operation is bad and probably was not indicated in the first place. Again, one must be able to determine the exact location of the disease before satisfactory segmental resection can be carried out.

We believe that pulmonary tissue should not be sacrificed unnecessarily and that when feasible a segmental resection should be preferred to a lobectomy. By the same token, we prefer this operation to thoracoplasty in most cases, and here



Segmental clock
(RIGHT LATERAL VIEW)

Fig. 7

I also mean in a large number of bilateral cases. With experience the operative risk can be nearly as low as that for thoracoplasty, with as high a rate of cure, better cosmetic results and pulmonary function. Should results of pulmonary function tests be slightly below par, this operation allows us to perform a decortication and to free an adherent lung-diaphragm component, so often causative.

We believe treatment should be applied fairly early in the disease, but preferably after a minimum of six months' bed rest and antibiotics. At this time, cases should be reviewed, and their segmental clock observed; if compensatory emphysema has appeared, the diseased segment should be removed if cavitary or solid.

We are not ready to discuss, let alone solve the problem of, the sputum–negative patient with a small nodule or cavity, or, as O'Brien[5] calls it, a small "nubbin" in an upper segment. If the recurrence rate in these cases is definitely 30%, perhaps we should operate upon more of them. Until we know for certain the fate of these patients–and it is important that we apply ourselves to discovering it–we must base our decisions on extraneous factors such as social condition.

TECHNIQUE

This is now pretty well standardized. Our cases are prepared by rest and antibiotics and when deemed ready by the medical division are presented for surgical evaluation. If the case is accepted, the cardiac and pulmonary functions are studied closely, together with other general surgical tests. The patient with a lesion amenable to a segmental resection is usually in good general condition and seldom presents a serious problem.

All cases are studied bronchoscopically. Streptomycin resistance tests are done, but we operate whether there is sensitivity or not. Patients are well instructed by the physiotherapist. A few words from the operating surgeon as to what will be expected of them for the first few days goes a long way in preparing a smooth postoperative course.

We routinely use the double-lumen Carlens tube, the choice of the anæsthetic agent being left to the anæsthetist. Voluntarily or not, we have rather narrowed his field because we like to use the cautery throughout the procedure. The lateral position is used, and no ribs are ever removed or cut for segmental resections. We believe the thoracic cage should be disturbed as little as possible and we have found it quite easy to carry out any procedure with only an intercostal spread. Just before incising the pleura, the lung is collapsed, which permits a better entry, and immediately a good evaluation of the pathology. The lung is soon re-expanded and carefully observed to see what segments remain atelectatic. Then the whole lung is carefully palpated and the surgical plan decided upon. The segmental arteries are tied and cut. The segmental bronchi are clamped temporarily and the lung is inflated. This gives us a very good idea of what to remove. The bronchi are cut, closed with interrupted, slightly inverting stitches of fine silk, nylon or cotton, and the stump pleuralized if possible. Lung tissue is reunited lightly over the bronchial stump. The veins are tied, and the segments dissected in a retrograde fashion while the lung is being moderately inflated. Slight bleeding and bubbling will occur; this is controlled with a gauze pack until the surgeon is ready for hæmostasis and small bronchial ties. Air leaks always remain, but they are surprisingly few if the intersegmental plane is entered. Drainage with a superior and an inferior tube is established. Negative suction is applied, registering at least 20 to 30 cm. of water. We often like to bring it up to 50 or 60 cm. All sponges are weighed in the operating room and blood is replaced as necessary. Usually not more than 40.5 gm. of sodium chloride is given postoperatively, along with 1,000 to 2,000 c.c. of 5% or 10% glucose.

The day following operation, the patient is expected to drink and eat. The tracheo-bronchial

tree is watched just as carefully as the blood pressure; any rise in temperature usually means retention of secretions. Patients are helped hourly in their coughing and at least a few times at night. Bronchial aspiration and even tracheotomy are quickly resorted to if judged necessary. The tubes are usually removed within 48 hours. One may be left in longer and the suction increased if there seems to be an important air leak.

Usually within a month these patients are discharged to the medical section or returned to their sanatorium for further rest.

We will now discuss a few figures pertaining to our 34 cases of segmental resection. The oldest case was operated on two years ago, the last case only three months ago. Needless to say, we are not speaking of long-term results.

Mortality.—(1) Operative (within 60 days of operation): One out of 34 (rate 2.9%). (2) Late (from two years to three months after operation): None. (3) Total mortality rate: 2.9%.

Morbidity (B.P.F.).—(1) Early: One out of 34 cases (rate 2.9%). (2) Late: None. Total B.P.F. rate 2.9%.

Empyemas.—(1) Early: One out of 34 cases (rate 2.9%). (2) Late: None. Total empyema rate 2.9%.

Hæmorrhages.—None in 34 cases.

Atelectasis.—Eight of 34 cases (rate 23.9%).

Reactivations.—Seven of 34 cases (rate 20.5%). All cases of reactivation but one had postoperative atelectasis. Only 2 patients who had postoperative atelectasis did not show reactivation.

Bronchograms.—Two patients in this series had preoperative bronchograms (Lipiodol). The first, who was bronchographed two months preoperatively, developed massive postoperative atelectasis, B.P.F., and died. The second, bronchographed 10 days preoperatively, developed atelectasis, reactivated, became sputum-positive, and was readmitted for further surgery.

Our one fatality should not have happened. The patient was a young woman with a small left upper lobe cavity. For some reason unknown to us, a bronchogram of the left base was taken two months preoperatively. At the time of operation there was considerable residual Lipiodol. She developed marked postoperative atelectasis, and was aspirated and bronchoscoped many times. About 15 days after operation she developed a broncho-pleural fistula, which was immediately drained, and a small thoracoplasty was performed. Two days later, she seemed to be pulling through. While a bronchial aspiration was being done in her bed, her bronchial tree became flooded, the suction pump blocked and she died of anoxia. Instantaneous heart massage was ineffective, as an adequate airway could not be re-established soon enough. An accumulation of small mishaps in a good cause led to her death. We do not want to imply that Lipiodol is terribly dangerous in tuberculous surgical cases. Let us simply say that we do not like it.

As regards morbidity, our figures are high for postoperative atelectasis and reactivation. Our consolation is that we were very fortunate with so much atelectasis in having had only one broncho-pleural fistula. Our figures seem to establish a close relation between postoperative atelectasis and reactivation. We believe this to be correct and have undertaken all possible methods to prevent this atelectasis.

We have found the following to be of help. (1) Frequent inflation of lung during operation, and in between times continuous bronchial aspiration. (2) Immediate postoperative complete bronchial aspiration. (3) Higher suction application to drainage tubes. (4) Intensive physiotherapy. (5) Breathing exercises and controlled coughing. (6) Aerosol therapy. (7) Bronchial aspiration as deemed necessary.

Sputum examination at the time of operation showed that 27 out of 34 cases were positive. None of the 7 negative cases has presented the slightest complication.

Of the 33 patients now living, the 7 negative ones have remained negative, and 20 of the 26 others became negative at once, while a further 2 became negative with further surgery. Hence there are now 29 sputum-negative patients (87.8%).

Of the remaining 4 sputum-positive cases, one patient has been accepted for further surgery, and in the other cases it is too early to decide.

CONCLUSION

With further experience we believe we can match the low rate of complications of thoracoplasty. We certainly can give the patient better pulmonary function, less deformity, and a better outlook on life. With the co-operation of the medical men, we think we can shorten sanatorium stay, which after all is no small factor in our economy. We believe in resecting only diseased tissue. If we adhere to this, we will be

rid of residual spaces, empyemas, post-resection thoracoplasties and some broncho-pleural fistulas.

If we extend this type of resection too far, we are likely to have trouble. Where the line of demarcation between good and bad conservatism lies is very difficult to say.

SUMMARY

We have presented our experience with 34 cases of segmental resection for pulmonary tuberculosis. Our views on the problem in general have been set out.

Our method of selecting cases has been mentioned.

Our vital statistics have been given and explained.

Our preference for this operation, when indicated, has been expressed.

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SUBTOTAL GASTRIC RESECTION FOR MASSIVE UPPER GASTROINTESTINAL HÆMORRHAGE IN THE ABSENCE OF DEMONSTRABLE LESION*

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A REVIEW of several reports in the literature concerning the treatment of upper gastrointestinal hæmorrhage indicates that it is frequently necessary to resort to emergency operative treatment in an effort to control bleeding which is massive and which continues despite conservative therapy.[1 to 5] Peptic ulcer is responsible for approximately 85% of gross hæmorrhages from the upper gastrointestinal tract, and this is dealt with by a direct surgical attack upon the bleeding vessel with subtotal gastric resection when possible.[6] However, not infrequently the decision to operate is made and the abdomen is opened only to find that no causative lesion can be found by inspection, palpation and, often, by gastrotomy. It is in these circumstances that subtotal gastric resection has been carried out, on the basis that the stomach and/or the first part of the duodenum is almost certainly the site of bleeding even though a gross lesion may not be detectable.

From time to time, over a period of several years, this situation has arisen in cases of upper gastrointestinal hæmorrhage at the Royal Victoria Hospital. A review of the cases falling into the aforementioned category, in the eleven-year period from the beginning of 1942 to the end of 1953, has been made. Brief abstracts of the case histories of 18 patients appear later in this paper.

Rigid criteria were applied in the selection of these 18 cases encountered in the eleven-year period so that none was included in which the lesion responsible for the hæmorrhage could be detected at the time of emergency laparotomy or by preoperative investigation when circumstances permitted studies to be carried out.

Except in cases of very massive, acutely exsanguinating hæmorrhage, it is usually possible to maintain the patient by means of replacement blood transfusions and other conservative measures for a period of time sufficient to permit certain studies to be completed in clarification of the diagnosis of at least the site of the lesion causing the hæmorrhage. It is essential to determine whether the site of hæmorrhage is situated above the diaphragm or below it. Once it can be shown that there is no lesion of the mouth, nasopharynx, paranasal sinuses, pharynx, larynx or œsophagus responsible for the hæmorrhage, the problem resolves itself to the extent that the bleeding must be from the upper gastrointestinal tract. To this end the elicitation of a detailed history of the illness and the performance of a careful physical examination are essential; the points of prime importance need not be enumerated here.

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Although no symptoms or signs of an œsophageal lesion, such as tumour or varices, may be evident, it is still absolutely necessary to exclude lesions of the œsophagus. A barium swallow with fluoroscopic and radiographic examination is usually sufficient to exclude the presence of œsophageal varices or other lesion likely to lead to massive hæmorrhage. At times, such an examination may also demonstrate a gastric or duodenal lesion despite the occurrence of active bleeding at the time. The objection that such a patient is often too critically ill to permit x-ray examination is rarely valid. If the site of the lesion is known with reasonable certainty (for example, recently proven peptic ulcer of stomach or duodenum), diagnostic x-ray procedures are unnecessary. However, if a bleeding lesion of the œsophagus is overlooked, the whole train of therapeutic events will be unsuitable and therefore ineffective, whether conservative or surgical (for example, laparotomy). In certain instances it may be impossible to carry out an adequate x-ray examination of the œsophagus and the existence of bleeding œsophageal varices will still be in doubt. If this is the case, immediate œsophagoscopy is necessary to settle the point by direct inspection of the œsophageal mucosa.

If the situation is too acute to permit elective œsophagoscopy with local anæsthesia, preparation for laparotomy may be made and the patient given a general anæsthetic. Œsophagoscopy may then be carried out quickly and, if there is no œsophageal lesion present, laparotomy can be performed at once.

Gastric aspiration with a Levine-type tube is considered by some authors to be of considerable value in the prompt recognition of recurrence or continuance of bleeding.[7] It is felt that in some patients the site of hæmorrhage can be deduced from the association of continuing melæna with clear aspirated specimens. It must be realized that achlorhydria is frequently found when an acute peptic ulcer is bleeding.

As soon as it is determined that the site of bleeding is below the œsophago-gastric junction, one is confronted with the necessity of deciding which of three therapeutic alternatives is most advisable: (a) to carry on with conservative supportive treatment and blood transfusions alone; (b) to perform an immediate laparotomy with the intention of locating and dealing with the responsible lesion surgically before further, perhaps fatal, hæmorrhage ensues; (c) to carry on with conservative treatment for a time, observing the patient closely for signs of continuing hæmorrhage and deterioration, reserving laparotomy as a measure of desperation after conservative measures have obviously failed. The making of this decision on the treatment of massive upper gastrointestinal hæmorrhage will not be discussed here, for this paper is concerned primarily with the results obtained when emergency or urgent gastric resection was performed in a series of 18 cases in which no lesion could be demonstrated preoperatively or during the operative procedure.

CASE 1

Mr. H.H., age 33 years. On March 18, 1941, a subtotal gastric resection with exclusion of the pylorus was performed for intractable ulcer of the second portion of the duodenum which had bled intermittently. He was hospitalized again from April 22 to May 8, 1942, because of recurrence of gastrointestinal hæmorrhage. He was admitted in a state of shock, and multiple blood transfusions were given. Gastroscopic examination on April 29 showed some erythema at the gastro-enterostomy stoma and no ulceration was seen. On April 27, a barium meal examination showed no evidence of stomal ulcer, and on May 6 a barium enema examination was negative. With conservative therapy the hæmorrhage ceased and the patient was discharged without the site of bleeding having been determined. On September 12, 1942, he was admitted for the third time in a state of hæmorrhagic shock from another massive gastrointestinal hæmorrhage. Another barium meal x-ray examination on October 5 showed a normal, functioning gastroenterostomy with no evidence of ulcer. The hæmorrhage ceased spontaneously and the original hæmoglobin level of 20% was raised by blood transfusions. On September 23 a laparotomy was performed. No evidence of peptic ulcer or other source of bleeding could be found. The pylorus and first part of the duodenum, which had been excluded in the previous operation, in March 1941, were removed and part of the gastric remnant was excised to afford an approximately 90% gastric resection. Examination of the surgical specimens revealed some inflammation of gastric wall but no sign of persistent, recurrent or stomal ulcer in the stomach, jejunum or duodenum. The postoperative course was uneventful and the patient was discharged on October 6, 1942, for further convalescence, with a hæmoglobin level of 66% and red cell count of 3,350,000. Subsequently he developed pulmonary tuberculosis which was treated at another hospital. So far as is known, hæmorrhage has not recurred.

CASE 2

Mr. D.S., age 55 years. This patient was admitted on June 10, 1942, because of massive melæna and evidence of extensive gastrointestinal hæmorrhage. Gastric analysis showed the maximum free acid to be 34 units and the total acid to be 56 units. The hæmoglobin level on admission was 55%. Both a barium meal and a barium enema examination showed no lesion. Bleeding ceased; he improved with conservative treatment and was discharged on June 23, 1942. On November 3, 1942, he was readmitted complaining of continuing intermittent melæna following his discharge in June, with an exacerbation of weakness, shortness of breath and tightness in his chest on the day of admission. Examination revealed a mild state of hæmorrhagic shock and blood was found in the stool. He was treated by transfusions of blood and conservative supportive measures for four

days, but there was evidence of continuing hæmorrhage. On November 7, 1942, laparotomy was performed and no intra-abdominal lesion could be found. Subtotal gastric resection and appendicectomy were performed. Grossly, the specimen showed several bleeding points in the gastric mucosa. Microscopic examination showed the presence of œdema and vasodilatation in the submucosa of the stomach. In March 1954, this patient stated that he had had no further bleeding from his gastrointestinal tract; he had had no digestive complaints and had been able to carry on with his normal activities ever since his convalescence in 1942.

CASE 3

Mrs. M.P., age 60 years. This patient was admitted to the Medical Service on July 2, 1942, and transferred to the Surgical Service on July 3. She had vomited blood and had passed tarry stools. Her hæmoglobin level was 65% and transfusions of whole blood were given. After admission on July 2, she vomited large quantities of blood and her blood pressure fell to shock level. This was controlled by transfusions of blood but on July 3 she vomited a large quantity of blood on two occasions, with a second drop in blood pressure and elevation of pulse rate. A surgical consultation was held, and she was transferred to the Surgical Service with a hæmoglobin level of 57% and her condition considerably worse than on admission. Laparotomy was performed on the evening of July 3, 1942. Abdominal exploration revealed no lesion, but the duodenum and pylorus were adherent to a scar resulting from a cholecystectomy some years previously. Subtotal gastric resection was carried out. Grossly, the specimen showed evidence of gastritis with slight erosions of the mucosa on the lesser curvature. There were many sites of oozing of blood from the gastric mucosa. Microscopic examination confirmed the presence of gastritis and mucosal erosions, and a diagnosis was made of hæmorrhagic gastritis without ulceration. The pyloric mucosa was thickened and irregular. Postoperatively, many transfusions of blood were given. The patient developed fever, lethargy and parotitis, and on the seventh postoperative day drainage from the wound suggestive of duodenal fistula appeared. This was treated by local aspiration and Levine tube gastric suction. There was no evidence of generalized peritonitis. The patient was maintained by means of parenteral fluid therapy but gradually became stuporous, lost consciousness on the tenth day and died on the twelfth postoperative day. Post mortem examination revealed the following abnormalities: acute hæmorrhagic gastritis, acute ulcer of the fundus of the stomach (1 mm. in diameter), perforated duodenal stump, subtotal gastric resection, localized peritonitis, thrombosis of external iliac and femoral veins, generalized arteriosclerosis, arteriosclerotic scarring of kidneys, fatty metamorphosis of liver, old cholecystectomy, and fibrous adhesions of the peritoneal cavity.

CASE 4

Mr. A.C., age 61 years. This patient was admitted to the Medical Service on February 16, 1943, and transferred to the Surgical Service on February 17. He was admitted with the complaints of chronic headaches, bloody, malodorous stool, occasional feeling of heaviness in the abdomen after meals, weakness and vomiting of blood for one day. Examination revealed a moderate degree of hypotensive hæmorrhagic shock and he was transferred to Surgery with a hæmoglobin value of 36% and a falling blood pressure, despite transfusions of blood. After February 17 he received several blood transfusions and was subjected to laparotomy. Exploration of the abdomen revealed no lesion to account for the bleeding and subtotal gastric resection was performed. The specimen showed hæmorrhagic gastritis, with hyperæmia and hæmorrhagic extravasation in the duodenum but no ulcer or erosion. In March 1954 this patient stated that he had had no further bleeding from the gastrointestinal tract, that he had had only occasional mild digestive complaints and that he was able to carry on his normal activities perfectly well.

CASE 5

Mr. G.G., age 36 years. This man was admitted on March 4, 1943, with a history of having had a peptic ulcer diagnosed clinically in 1935 and in 1940, for which he was treated conservatively. He had had two episodes of hæmatemesis, in January 1943 and in late February, with tarry stools after each episode. During the two weeks before this admission he had had hæmatemesis almost daily. Barium meal x-ray examination on March 6 revealed findings suggestive of a prepyloric ulcer but no definite ulcer crater could be identified. On March 10, 1943, laparotomy was performed. Abdominal exploration revealed the presence of a Meckel's diverticulum with no complicating lesion. There was a suggestion of scarring of the duodenal wall but no ulcer could be palpated. Subtotal gastric resection and excision of the Meckel's diverticulum was carried out. Pathological examination of the specimen showed no ulcer in the Meckel's diverticulum and the stomach was normal apart from mild submucosal inflammatory changes. No erosion or ulceration of the duodenum was present. This patient has not been readmitted since and a letter sent to him inquiring about the state of his health in March 1954 was not answered.

CASE 6

Mr. J.K., age 55 years. This man was admitted to the Surgical Service on March 26, 1943, with the complaints of loss of weight over a three-week period and hæmatemesis on one occasion three weeks before admission. A barium meal on March 27 was negative and an intravenous pyelogram on March 29 showed bilateral hydronephrosis. A barium enema examination on April 5 was negative. A urologist consulted on April 1 gave the opinion that the patient had prostatism and mild bilateral hydronephrosis. His coagulogram was normal. On April 4, 1943, a laparotomy was performed and no lesions were found, apart from slight thickening of the gastric walls and rugæ. Subtotal gastric resection was performed and he was discharged on April 24. The specimen showed no evidence of ulcer or tumour but there was gross and microscopic evidence of exudative gastritis. The patient was readmitted three times subsequently to the Urological Service for urological treatment. There was no further bleeding from the gastrointestinal tract and his symptoms were completely relieved. The patient stated in March 1954 that he had had no further bleeding, that he had had no digestive complaints and that he was able to carry on his usual activities without difficulty.

CASE 7

Mrs. M.G., age 55 years. This patient was admitted to the Surgical Service on October 9, 1945, because of massive hæmatemesis and melæna accompanied by severe shock and collapse. The patient had had several previous hospital admissions for gynæcological conditions and the clinical diagnosis of duodenal ulcer had been made on two occasions, in 1928 and in 1933. In 1933 she was transferred from Medicine to Surgery for a diagnostic laparotomy, at which time chronic pancreatitis alone was found. In 1936 she had had massive hæmatemesis and melæna; the source of bleeding was not determined. In 1936 an exploratory laparotomy for gastrointestinal bleeding was followed by peritonitis owing to accidental laceration of small bowel. Still later, during the same admission, this was surgically drained and before the patient was discharged appendicectomy was performed. In 1937 massive hæmatemesis and melæna recurred and she was admitted, but the source of

the bleeding was not determined. In 1944 she had massive hæmatemesis once more but the source was again not determined. A barium meal x-ray examination on October 17 showed no sign of peptic ulcer and on October 23 a chest film was normal. Although conservative supportive therapy with blood transfusions controlled the hæmorrhagic shock and bleeding slowed or stopped, the source of hæmorrhage could not be determined. On October 25 exploratory laparotomy was performed. There were no signs of ulcer or tumour. Subtotal gastric resection and repair of the old incisional hernia was carried out. She was discharged on November 13, 1945. A specimen showed no lesion on examination in the Department of Pathology. She did not reply to a questionnaire sent to her in March 1954.

CASE 8

Mr. J.C.B., age 58 years. This man was admitted to the Medical Service on January 3, 1946, because of the following acute symptoms: vomiting of undigested meal after a cocktail party 24 hours prior to admission, recent weight loss of seven pounds, attacks of indigestion for years and hæmatemesis on both the evening and morning previous to admission. Clinically, the patient was in profound hæmorrhagic shock. Several blood transfusions were given and the patient was transferred to the Surgical Service. An emergency laparotomy was performed on January 4, 1946. No lesion was found, but the stomach contained blood clots. Subtotal gastric resection was carried out. The specimen showed hyperæmia of the gastric mucosa with some œdema and exudative serositis. The patient was discharged on January 25, 1946. In February 1954, he stated that he had had no recurrence of his previous bleeding and was in good health.

CASE 9

Mr. O.M., age 53 years. This patient was admitted to the Surgical Service on September 1, 1948, because of post-prandial distress and intermittently tarry stools over a period of 11 years. Physical examination, routine investigation, and barium meal x-ray examination revealed no abnormality. A barium enema demonstrated the presence of diverticulosis of descending and pelvic colon. The patient was discharged on September 9, 1948, and advised to follow a low-residue diet and to take antispasmodic agents. The next day he was readmitted because of gross melæna, collapse and pallor. His hæmoglobin level was found to have dropped from 98% to 33% and he was in a state of profound hæmorrhagic shock. Multiple blood transfusions were given rapidly but the patient continued to bleed intermittently for another 72 hours, then the bleeding stopped and the hæmoglobin level rose gradually to 60% with further transfusions. On September 14 a laparotomy was performed. No lesion was found apart from the Meckel's diverticulum which was free of any lesion. Subtotal gastric resection was performed and the Meckel's diverticulum was excised. Examination of the specimens demonstrated no lesions. The patient replied to a questionnaire in March 1954, and stated that he had had no further bleeding since his operation and that he was carrying on his normal activities.

CASE 10

Mrs. L.H., age 42 years. This lady was admitted to the Medical Service on February 20, 1949, because of the occurrence of three massive gastrointestinal hæmorrhages, with hæmatemesis and melæna, during the previous four years. On February 22 and 24 barium meal examinations revealed no abnormality. She was transferred to the Surgical Service on February 25, and on March 1 an exploratory laparotomy was performed. No lesion was found within the abdomen. Subtotal gastric resection was performed. Examination of the specimen revealed hyperæmia and œdema of the stomach with hæmorrhagic extravasations. This patient replied to a questionnaire in March 1954, and stated that she had had no further bleeding since her operation and that she has been running her household without undue difficulty.

CASE 11

Mrs. J.B., age 50 years. This lady was admitted to the Medical Service on March 10, 1949, complaining of an episode of abdominal pain, weakness and melæna two years previously and of acute symptoms of a few hours' duration, including weakness and dizziness, tarry stools, slight abdominal pain with nausea and fainting attacks when attempting to get up to go to the bathroom. The patient had symptoms of massive hæmorrhage with only mild hæmorrhagic shock, and many blood transfusions were given to raise her initial hæmoglobin level of 36% to 78% by March 28. The bleeding gradually stopped and by April 5 her hæmoglobin level was 84%. On March 22 a barium meal x-ray examination revealed no lesion. The patient was transferred to the Surgical Service on April 8 and laparotomy was performed on April 9. As no lesion was found, subtotal gastric resection was carried out. The specimen showed no lesion. The patient replied to a questionnaire in March 1954, stating that she had had no further bleeding from her gastrointestinal tract and that she was carrying on her normal activities.

CASE 12

Mr. G.Y., age 64 years. This man was admitted to the Medical Service on April 20, 1949, with a history of melæna and with a hæmoglobin level of 15%. He was transferred to the Surgical Service five days after admission, during which time he had received 4,000 c.c. of whole blood. On April 19 a chest film and barium enema had both been found negative. On April 22 subtotal gastric resection was carried out for two lesser curvature gastric ulcers discovered at operation. The postoperative course was smooth. He was readmitted on May 19, 1949, because of the recurrence of melæna and hæmorrhagic anæmia, with a hæmoglobin level of 40%. Treatment included many blood transfusions, with rapid improvement in the patient's condition. He was transferred to the Surgical Service on June 3, 1949, because of the persistence of melæna. On June 7 laparotomy was performed because of the continuing hæmorrhage. No evidence of stomal ulcer was found at operation. Most of the gastric remnant was resected, leaving a cuff of gastric wall about 4 cm. long. The specimen showed evidences of exudative gastritis with areas of granulomatous reaction about foreign bodies, presumably the non-absorbable sutures of the first operation. The postoperative course was complicated by pulmonary infarction, for which the femoral veins were ligated under local anæsthesia. His convalescence was stormy and he was unable to take his feedings properly. On June 21 a barium-swallow x-ray examination demonstrated a leak at the gastroenterostomy site. Because of this leak, a jejunostomy was established on June 25 for feeding purposes. The leak healed, as proved by further x-ray studies, and feedings were resumed; the patient gradually gained weight before being discharged on August 5, 1949. He was readmitted to the Surgical Service on November 6, 1949, because of recurrent massive gastrointestinal hæmorrhage. His hæmoglobin level on admission was 18% and he was in a state of profound shock. Transfusions were given and he slowly improved and began to take some food orally. On November 12 he began to bleed again and despite transfusions he died on November 13 of continuing hæmorrhage. An autopsy was performed with the following findings: chronic gastritis, enteritis, and colitis (diffuse with the cause unknown), ulceration of intestinal mucosa (patchy, involving the cæcum and descending colon), hæmorrhage into the

gastrointestinal tract, ascites, chronic fibrinous peritonitis, fibrosis of the myocardium, and thrombosis of the pelvic veins.

CASE 13

Mr. L.M., age 62 years. This patient was admitted to the Medical Service on February 22, 1950, in a very serious condition. He was comatose, in a state of hypotensive shock, and unable to answer questions, so that the history had to be obtained from his relatives. He had been well until February 12, when, while eating his supper of meat and potatoes, something seemed to stick in his throat. His throat became quite painful and swollen on the following day. He was able to swallow dry bread but could eat very little because of dysphagia. The swelling disappeared within four to six days. On February 19 he became unable to take food by mouth, but there was no known fever or chills. Earlier on the date of admission the patient had a severe headache and at 11.00 a.m. developed severe abdominal cramps and between then and 4.00 p.m. had four bowel movements of unknown type or quantity. At 6.00 p.m. he vomited about one pint of fresh blood and fainted. A doctor was called and the patient was brought by ambulance to the hospital. After 6.00 p.m. he had several episodes of hæmatemesis, a small quantity of blood appearing each time. A transfusion of blood was begun immediately upon arrival and was continued throughout the night and an infusion of glucose in saline continued after 6.00 a.m. on February 23. At 7.00 a.m. the patient vomited blood twice and another transfusion was begun. At 9.30 a.m. he vomited at least 500 c.c. of fresh blood. His blood pressure dropped and his condition became critical. Rapid transfusion was given and a gastric tube was passed and suction applied to it. Hæmatemesis continued and by 10.30 a.m. the blood pressure was not measurable or the pulse detectable. The patient was then transferred to the Surgical Service, the tentative differential diagnosis being bleeding peptic ulcer, œsophageal varices with hæmorrhage, or pharyngeal or œsophageal injury. Large quantities of blood were given by transfusion and exploratory laparotomy was performed at 12.00 noon on February 23. At the beginning of the operation the blood pressure was 60/20 mm. Hg and by 1.00 p.m. it was 120/56 mm. Hg. No lesion was detected in the abdomen and there was no evidence of portal hypertension. Subtotal gastric resection was carried out. The patient continued to bleed and it was realized that the site of the hæmorrhage must be in the œsophagus. Œsophagoscopy was performed at once in the operating room but it was impossible to inspect the œsophagus adequately because of massive bleeding, which obscured vision. The œsophagus was packed, but rapid hæmorrhage continued and the patient died in the operating room. The resected specimen of the stomach revealed no lesion. Autopsy findings included: ulceration of the œsophagus 5 cm. below the hypopharynx (bilateral), with penetration of the œsophagus into the right para-œsophageal tissues, erosion of the right thyrocervical arterial trunk, massive hæmorrhage into the œsophagus, shock, and early lower nephron nephrosis.

CASE 14

Mr. O.S., age 39 years. This man was admitted to the Medical Service on August 1, 1951, because of upper gastrointestinal bleeding. He was treated by blood transfusions, which raised his hæmoglobin level to 87% by August 16, at which time he was transferred to the Surgical Service. He had had one previous admission for gastroenteritis in 1941. A barium-meal examination revealed no evidence of peptic ulcer or other lesion. In view of the history of upper gastrointestinal bleeding, and upper abdominal pain suggestive of penetrating duodenal ulcer, laparotomy was performed on August 18, 1951. No lesion was found on exploration of the abdomen, and subtotal gastric resection was performed. Examination of the specimen revealed no lesion. The patient stated in March 1954 that he had had no further bleeding from his gastrointestinal tract and that he had been carrying on his normal activities ever since his operation.

CASE 15

Mr. J.D.H., age 39 years. This man was admitted to the Surgical Service on February 23, 1952, with a history of a massive upper gastrointestinal hæmorrhage in 1949, with x-ray evidence suggestive of duodenal ulceration at that time. The complaints on this admission were vomiting of dark red blood two and one-half hours before admission, weakness and fatigue for two days, borborygmi for one day, dark stools followed by a dark red stool of large volume on the day of admission, and a faint feeling with partial collapse after the hæmatemesis and just before admission. He was in a mild degree of hypotensive shock and there was marked pallor. On February 27 a barium-meal x-ray examination was performed after several transfusions had been given and bleeding had decreased. This demonstrated irritability of the duodenal cap but no ulcer crater was identified. Multiple transfusions of whole blood were given and on March 1 laparotomy was performed. Complete abdominal exploration revealed no lesion and no evidence of ulcer of the stomach or duodenum was found. Subtotal gastric resection was carried out. The pathologist reported that the stomach and duodenum showed hyperæmia and œdema, but no ulceration or tumour was found. He was discharged with no further bleeding on March 13, 1952. In February 1954 this patient stated that he had had no further bleeding since his operation, and that he was carrying on his usual activities.

CASE 16

Mr. L.L., age 68 years. This man was admitted on January 30, 1953, with complaints of weakness, loss of weight, pallor, and the presence of dark stools, diarrhœa, and blurring of vision for one day before admission. On February 2 a chest film was normal and a barium-meal examination showed an irregularity of the fundus of the stomach suggestive of an expanding lesion at this site. On February 6 laparotomy was performed and revealed no demonstrable lesion. The abdomen was closed. Bleeding continued and on February 10 œsophagoscopy showed blood welling up into the lower end of the œsophagus from the stomach, but no lesion was present in the œsophagus itself. Bleeding continued, requiring numerous blood transfusions. On February 17 subtotal gastric resection was performed and the specimen revealed hæmorrhagic extravasations and mild exudative gastritis. On admission his hæmoglobin level was 45% and by the day of partial gastrectomy—February 17—he had received blood transfusions totalling 11,500 c.c. and his hæmoglobin level was then 57%. Another 1,500 c.c. of blood was given during his hospital convalescence, the last transfusion being on February 22, making a total of 13,000 c.c. of blood given during his hospital stay. His hæmoglobin level on February 22 was 68%. He developed leakage of gastric contents from the wound but a barium swallow did not reveal a leak from the anastomosis. However, the stoma was blocked and no barium passed through it. Accordingly, a Levine tube was passed and fortunately it was possible to pass it through the stoma into the efferent jejunal loop and the patient was maintained on jejunostomy feedings. By March 10 barium-meal examination revealed no stomal obstruction and feedings were resumed. After a long, stormy convalescence he was discharged on March 26, 1953, feeling and looking reasonably well. In March 1954 this man stated that he had had no further bleeding from the gastrointestinal tract, and no complaints referable to his digestive system since his operation, and he was carrying on his normal activities.

TABLE I.

Case	*Patient*	*Sex*	*Age*	*Date of operation*	*Pathological report*	*Result*
1	H.H.	M.	33	Sept. 23, 1949	Inflammation of stomach	Good
2	D.S.	M.	55	Nov. 7, 1942	Œdema with gastric mucosa with dil. of vessels	Good
3	M.P.	F.	60	July 3, 1942	Hæmorrhagic gastritis	Died
4	A.C.	M.	61	Feb. 17, 1943	Hæmorrhagic gastritis	Good
5	G.G.	M.	36	March 10, 1943	Gastric submuc. inflam.	Good
6	J.K.	M.	55	April 4, 1943	Exudative gastritis	Good
7	M.G.	M.	55	Oct. 25, 1945	No lesion	Good
8	J.B.	M.	58	Jan. 4, 1946	Hæmorrhagic gastritis	Good
9	O.M.	M.	53	Sept. 14, 1948	No lesion	Good
10	L.H.	F.	42	March 1, 1949	Hyperæmia, œdema of stomach, extravasation	Good
11	J.B.	F.	50	April 9, 1949	No lesion	Good
12	G.Y.	M.	64	April 22, 1949	Exudative gastritis	Died
13	L.M.	M.	62	Feb. 23, 1950	Normal stomach	Died
14	O.S.	M.	39	Aug. 18, 1951	No lesion	Good
15	J.H.	M.	39	March 1, 1952	Hyperæmia, œdema stomach and duodenum	Good
16	L.L.	M.	68	Feb. 17, 1953	Exudative gastritis, extravasation	Good
17	D.A.	F.	37	March 28, 1953	Ectasia of gastric submucosal vessels	Good
18	M.B.	M.	63	Oct. 2, 1953	Hyperæmia, œdema stomach	Good

Average age: 51.1 years. Males: females: 14:4.
Postoperative mortality rate: 16.6%.
Recurrence of hæmorrhage in survivors:—one case (No. 12).
Incidence of hypotensive shock on admission: 44.4%.

Case 17

Miss A.D., age 37 years. This patient was admitted to the Medical Service on March 19, 1953, because of tarry black stools, noted for four days in succession, and a previous episode of melæna on March 7, 1953. Physical examination was negative except for pallor. A barium-meal x-ray examination was negative on March 20. She was given transfusion of blood and transferred to the Surgical Service on March 27. On March 28, laparotomy was performed and no abnormality was found apart from a small whitish area on the anterior wall of the first part of the duodenum. Subtotal gastric resection was performed. The pathologist reported that the specimen showed only ectasia of the veins in the gastric submucosal layer. Her postoperative course was smooth and she was discharged on April 8, 1953. In March 1954 this patient stated that one month after discharge she had had a very slight hæmorrhage, producing a slightly darkened stool which was positive for occult blood. Since then there had been no further bleeding. She was able to carry on her normal activities.

Case 18.

Mr. M.B., age 63 years. In March 1953 this man had been admitted and a cholecystectomy performed for cholelithiasis. No other intra-abdominal lesion was detected at that time. He was admitted again on October 2, 1953, complaining of having fainted while straining at stool on September 23, of having vomited on September 23, and of having tarry stools from September 24 to 26. Fainting and incontinence of tarry stool in the outpatient department on October 1, 1953, led to his emergency admission. A barium-meal examination had been done on September 30, revealing no lesion. He was in a mild state of hypotensive shock with marked pallor at the time of admission. He was treated by daily transfusions of blood and on October 14 laparotomy was performed. Exploration revealed no abnormality of the stomach and duodenum but diverticulosis was noted as well as a polyp in the pelvic colon. Subtotal gastric resection and excision of the polyp were carried out. The pathologist reported hyperæmia and œdema of the stomach and adenocarcinoma in the polyp from the pelvic colon. On the tenth postoperative day, after the abdominal wound drain was removed, the patient complained of nausea, had hiccups and vomited after eating his meals. This state persisted for one week and the patient became ambulatory on October 31, 1953. Vomiting of food after eating persisted and on October 31 a barium meal demonstrated complete obstruction to the flow of barium through the stoma. Levine tube gastric suction was established and he was given parenteral fluids for two days as well as blood transfusions. Oral feedings were then resumed and taken very well, although he had occasional post-prandial vomiting for some days. He was discharged on November 16, 1953, for convalescence. In March 1954, this patient stated that he had had no further bleeding from the gastrointestinal tract.

Discussion of Results

There were three deaths in this series of 18 cases in which gastric resection for upper gastrointestinal bleeding without demonstrable lesion to account for it was carried out. This is a mortality of 16.6%. In none of the other 15 patients has significant hæmorrhage been reported since subtotal gastric resection was performed.

In Case 3 death was due to peritonitis caused by perforation or leakage of the duodenal stump. In Case 12 death resulted from recurrent massive hæmorrhage owing to gastritis, enteritis and colitis with multiple ulcerations. In Case 13 death was due to continuing massive hæmorrhage from an ulcer at a high level in the œsophagus, probably due to erosion of the œsophagus and thyrocervical arterial trunk by a foreign body swallowed several days previously (probably a bone fragment). This case involves an error in diagnosis of the site of hæmorrhage, and illustrates what serious consequences may follow such an error.

In the 15 cases with a successful outcome, 25% or less of the stomach remained after operative

treatment was completed. In Case 1 excision of the pylorus and duodenal stump was carried out along with further partial resection of the gastric pouch remaining after previous gastric resection, with exclusion of the pylorus, for duodenal ulcer.

In none of the 18 cases was a definite peptic ulcer or carcinoma identified in the gross or microscopic examinations of the surgical specimen. In Case 16 laparotomy and gastrotomy ten days previously had failed to reveal a bleeding lesion, indicating, in this instance, the futility of relying entirely upon gastrotomy for a definitive demonstration of the lesion responsible for hæmorrhage.

CONCLUSIONS

It is felt that, after suitable preliminary investigations to exclude a source of bleeding above the œsophagogastric junction, subtotal gastric resection is justified in the treatment of massive upper gastrointestinal hæmorrhage when careful abdominal exploration fails to demonstrate a causative lesion. In view of the fact that hæmorrhagic gastritis is often the lesion in these cases, it would seem advisable to perform vagotomy at the time of the gastric resection further to eliminate the acid-peptic digestive factor which is of so much importance in the production of peptic ulcer and acute mucosal erosion.[8, 9]

We are grateful to Dr. G. Gavin Miller, Dr. John Armour and Dr. Howard L. Dawson for inclusion of case histories of their patients in this series.

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THE IMPORTANCE OF THE BACILLARY STATUS*

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TUBERCLE BACILLI in the tissues may cause the clinical disease tuberculosis and the presence of bacilli in secretions from the body is indicative of active disease, which is a hazard for the patient and a danger to his associates. Too often the patient, and occasionally even his physician, is satisfied with a report of x-ray findings which are apparently satisfactory, forgetting that the radiograph does not tell all and indeed, by itself, may even give false evidence.

It is generally accepted and is more or less true that the earliest change from normal in a tuberculous individual is the indication in a chest radiograph of an infiltration in the lung parenchyma or change in the hilar region. It is not true that such a change should always be accepted as of tuberculous etiology, but rather that the finding should be subjected to clinical evaluation. Of the technical procedures employed, the tuberculin test and the determination of bacillary status are the most important, but should be supplemented by clinical history and physical examination.

The bacillary status of a patient is of importance in arriving at a diagnosis, in assessing the results of treatment, and in determining when the disease has reactivated.

It has been estimated that, if one can demonstrate the presence of tubercle bacilli by staining a direct smear of the sputum, there must be approximately 100,000 bacilli in every cubic centimetre of the sputum. If smaller numbers are present, concentration of the sputum will permit detection of as few as 500 organisms per c.c. A further refinement is culture, which will demonstrate a growth if as few as 50 organisms are present per c.c. of sputum.

Guinea-pig inoculation has an accuracy equal to that of laboratory culture but it is used infrequently because of the difficulty of maintaining a satisfactory stock of suitable animals. On occasion, however, it is required to demonstrate the

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virulence or disease-producing properties of tubercle bacilli suspected of being attenuated by prolonged and presumed adequate forms of treatment, or to help identify acid-fast bacilli suspected of being non-pathogens.

There is an impression abroad that if the patient states that he has no sputum he cannot be suffering from open tuberculosis. It must be remembered that part of pulmonary function is clearing secretions from the bronchial tree. These secretions are not noticeable unless in abnormal and appreciable amount, under which conditions such secretions are called sputum. The absence of sputum does not mean that a tuberculous lesion is closed.

Very small concentrations of tubercle bacilli may be identified from a study of gastric washings, thereby seeking out and identifying tubercle bacilli which have been swept into the pharynx by the respiratory cilia during sleep and swallowed unconsciously. It must be stressed that direct smear examinations of gastric washings are unsatisfactory, as a number of non-pathogenic acid-fast bacilli are normally present in certain foods and in tap water. Only positive cultures are significant, as the cultural characteristics of the pathogenic and non-pathogenic organisms are very different. It is desirable that this procedure be employed much more extensively than it is at the present time in arriving at an accurate diagnosis of tuberculosis.

It must be stressed that the only absolute criterion of the presence of tuberculosis is the demonstration of tubercle bacilli or the examination of tissue removed at operation or autopsy. Unfortunately, tubercle bacilli cannot always be demonstrated, but it is clinical negligence not to try to identify them by careful search and by every means at one's disposal. This frequently means repeated examinations of sputum by methods of increasing accuracy: smears, concentrations, cultures and gastric washing if each preceding method yields negative results. To label wrongly a case of active tuberculosis as bronchiectasis, bronchopneumonia, bronchitis, tumour or sarcoid reflects discredit on the diagnostician, is unfair to the patient, and is hazardous to his contacts.

As the sputum becomes less heavily loaded with bacilli, more tests will yield false negatives. In other words, if a sputum smear is positive it is likely that the majority of smears studied will also be positive. This is not so in the case of concentrations and cultures when frequently only occasional specimens yield positive results.

Of 100 consecutive cases admitted to the Nova Scotia Sanatorium since January 1, 1953, only 17 showed sputum positive on direct smear. In these 17 cases, 34 specimens were examined and 33 or 97% were positive. In 18 cases smears were negative, but four of these were positive on concentration and seven were positive on culture, showing the value of these more sensitive tests.

All cases are not examined by means of direct smear. If the quantity of sputum is small and it is not very purulent, it is customary to start with concentrations and culture tests.

Of the same 100 cases, 19 showed the sputum positive on concentration tests. In order to find these 19 positive cases, 71 specimens were concentrated. Of these, only 33 or 46% were positive. Of the 68 cases with negative concentration tests, 23 yielded positive cultures.

Of the 100 consecutive cases, a total of 38 revealed positive cultures for tubercle bacilli. This required the examination of 179 specimens, of which 95 or only 53% were positive. Of the negative culture cases, two had positive gastric washings.

In the City of Halifax, during 1953, 15 of the new cases diagnosed were classified as minimal, active. Only four of these patients claimed to have sputum, of which two were positive on culture. Of the 10 without sputum, all had gastric washings performed and four or 40% of these had positive cultures. One claimed to have sputum, but both sputum and gastric washings were negative. Of four minimal cases classified as arrested, two had sputum which was negative on culture. Two were without sputum, but gastric washings were positive. Of 11 minimal cases classified as inactive, seven had sputum negative on culture and four had gastric washings negative on culture.

At this point, one should also stress the need for determining the sputum status in pleural effusion cases and also primary infections, which used to be called childhood infections. In a very appreciable number of cases, gastric washing cultures will be positive for tubercle bacilli.

Not only must one carry out repeated tests of increasing sensitivity in order to demonstrate the presence of tubercle bacilli, but scientific caution demands at least one confirmatory test. When hundreds of tests are being done in a laboratory, it is conceivable that a single positive test might

represent a laboratory error due to cross-contamination or mislabelling. This should not occur but is possible. To have this happen twice to the same person would be an extreme rarity and the third time a virtual impossibility. In arriving at a diagnosis, the confirmatory tests are mandatory.

It should be pointed out that the great majority of the patients come to the Nova Scotia Sanatorium for the purpose of undergoing chest surgery. They have received prolonged periods of treatment at other institutions before reaching the surgical "target point". It is not surprising, therefore, that in 41 of these 100 consecutive cases the presence of tubercle bacilli was not demonstrated in the specimens taken on admission. An additional nine did show tubercle bacilli in specimens examined later.

The bacillary status helps one to assess the results of treatment. A negative test does not necessarily mean that the treatment has been adequate and so may be stopped, but a positive test does mean definitely that treatment and sanitary precautions are still required. The patient remains a menace to himself and his associates.

Under extensive antimicrobial treatment and bed rest, much of the soft exudative disease will disappear. Frequently, the patient is left with solid areas of disease which, if not removed, will ultimately break down and discharge bacilli, or he may be left with bronchiectasis and disabling symptoms such as hæmoptysis or troublesome cough and sputum or disability due to bronchial stenosis and atelectasis. Such were most of our 41 negative sputum cases sent forward to the Sanatorium from other institutions.

Nine of them, however, had previously had recent extensive antimicrobial treatment with streptomycin, PAS and/or isoniazid. It should be stressed that these drugs remain in the system for variable periods of time and inhibit the viability of organisms still present. A negative sputum test within the first three months after the discontinuance of such drugs cannot be considered truly significant and must be supported by subsequent findings.

Bacteriological testing of sputum is still a relatively crude procedure. A confirmed positive finding is acceptable proof of the presence of disease. Negative or even repeatedly negative tests do not necessarily mean that the disease is inactive. A positive smear may reveal the presence of 100,000 tubercle bacilli in one c.c. of sputum, a concentration test 500 tubercle bacilli and culture as few as 50. But how about those patients with healing disease and with less than 50 bacilli? A sputum culture or repeated cultures may not reveal the bacilli, but they are there. If healing does not continue, the concentration of bacilli will increase and a so-called relapse will occur. This is why a patient must continue to "cure" even after the radiograph reveals the disease to be apparently healed and the sputum is apparently negative on culture. "Under 50" is not really negative.

In regard to relapses in those patients considered to have had inactive disease for long periods of time, it should be stressed that reactivation is not always shown by the x-ray examination of the chest. The lung parenchyma may be obscured by pleural reactions or by the overlying collapsed thoracic cage as in a thoracoplasty, or the activity may develop as a bronchial ulceration or as active tuberculous bronchiestasis which cannot be demonstrated on a routine x-ray film.

If chest x-ray examination is unaccompanied by a clinical evaluation of symptoms plus a determination of the sputum status by the most refined methods available, it may well be a useless procedure presenting false information. It is possible to have a satisfactory radiograph in the presence of strongly positive sputum, but it is not possible to have a satisfactory state of health in the presence of these tubercle bacilli in secretions from the lungs.

Finally the significance to the patient of these procedures must be remembered, together with the fact that patients' attitudes toward tuberculosis have greatly changed. This is made manifest in many ways; for instance, by the almost complete co-operation of the public in having x-ray surveys and undergoing the resulting investigations required; and by the practically universal permission for tuberculin testing of school children, with the follow-up of positive tuberculin reactors and investigations for the sources of infection. The younger age groups, at least, have a healthy and aggressive attitude toward the control of tuberculosis and are co-operative in direct proportion to the understanding that each has of his or her disease. In any discussion with a patient concerning pulmonary tuberculosis the importance of the bacillary status (both to the patient and his associates)

must be emphasized. If this is done, co-operation on the part of the great majority will be forthcoming immediately and they will submit to whatever tests or observations may be recommended by the physician.

SUMMARY

The search for tubercle bacilli in body secretions is an imperative part of any investigation of lung disease, of assessment of treatment results and of reassessment when watching for reactivation of tuberculosis.

Sputum smears, concentrations, cultures and gastric washings must be examined *repeatedly* until a positive test is found or one is satisfied that the secretions are really negative.

When the diagnosis is in doubt, a single positive finding is not sufficient. One or two confirmatory positive findings are mandatory.

A negative sputum test in less than three months following the discontinuance of antimicrobial therapy is of tentative significance only and requires later confirmation.

The evaluation of a known case of tuberculosis by means of x-ray examination *alone* is dangerous and borders upon professional negligence.

CARDIO-PULMONARY DISTURBANCES IN THORACIC SURGERY

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DURING the last two and a half years 243 thoracoplasties, 264 pulmonary resections and 6 decortications were performed at Laval Hospital, Quebec. As anæsthetists, we were able to observe various cardio-pulmonary disturbances before, during and after operation. We thought that the analysis of these problems might interest phthisiologists and guide them when proposing surgery for pulmonary tuberculosis.

BEFORE OPERATION

During the preoperative period, complete evaluation of pulmonary function, cardiac reserve and blood volume is imperative. Recent advances in the surgical treatment of diseases of the pulmonary and cardiovascular systems demand a deeper understanding of the function of these systems. Surgical treatment is being currently advocated for patients in whom respiratory and cardiac function are borderline. These patients' reserves should be fully and accurately evaluated before operation. According to the classification of Baldwin, pulmonary function studies may be divided into the mechanical or structural, and the alveolar-respiratory or physico-chemical. In mechanical tests the lungs are considered as bellows and the tests are either static in type (like assessment of vital capacity, inspiratory capacity, tidal air, expiratory reserve, residual capacity, or total lung volume) or dynamic (as in tests of walking, ventilation, maximum breathing capacity, or timed vital capacity). Alveolar respiratory tests are concerned with the quantity and quality of gaseous exchange at the inspiratory, alveolar, capillary and tissue levels. They include intrapulmonary gas mixing, diffusion tests and arterial blood studies.

Until recently, we had to limit our activities to ventilation tests. We are now beginning alveolar exchange studies. Our studies on 220 patients would indicate that pulmonary tuberculosis reduces pulmonary efficiency. The actual vital capacity was found to be 75% or less of the estimated vital capacity in 191 cases, or 87%. The actual maximum breathing capacity was found to be 75% or less of the estimated maximum breathing capacity in 159 cases, or 72%.

In evaluation of cardiac reserves, the venous pressure and circulation time are two very helpful tests. According to P. D. White, venous pressure is the criterion of function of the right ventricle. Normal venous pressure ranges from two to ten cm. of water; the critical level is 20 cm. of water. The clinical value of the circulation time is in the estimation of the degree of decompensation in any heart case, especially with left ventricular failure. The higher the figure expressing the circulation time, the greater is the degree of decompensation. Venous pressure was measured in 73 patients pre-

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operatively (Table I). In 10 patients (14%) venous pressure was found above 20 cm.; 48 patients (66%) had a pressure above 10 cm.; 15

TABLE I.

VENOUS PRESSURE (NORMAL 2 - 10 CM. H_2O)

Pressure	*No. of cases*	*Percentage*
Above 20 cm. H_2O	10	14%
Above 10 cm. H_2O	48	66%
10 cm. H_2O or below	15	20%
Total	73	100%

patients (20%) had a normal venous pressure. On the other hand, only 3% of our patients showed a prolonged circulation time. We made electrocardiogram tracings on 199 patients (Table II). Twelve showed right incomplete

TABLE II.

ELECTROCARDIOGRAMS

Findings	*No. of cases*	*Percentage*
Right axis deviation (strain)	21	11%
Left axis deviation (strain)	6	3%
Right incomplete bundle branch block	12	6%
Normal ECG	160	80%
Total	199	100%

bundle branch block, which is not too significant; 6 had left axis deviation with left heart hypertrophy; 21 showed right axis deviation with strain. Most of the patients with right heart hypertrophy had severe pulmonary insufficiency.

Moot's test is an additional good criterion for estimation of cardiac reserves. In this test the pulse pressure is multiplied by 100 and the figure obtained is divided by the diastolic pressure. It was done on 73 patients: 30 had figures below 40 mm. Hg, the normal being between 40 and 60.

It has been reported that in tuberculous patients the blood volume is often reduced. Some clinical signs may help in this field but we like to rely on laboratory tests. The dye method with Evans blue or P.V.P. has appeared to us to be highly satisfactory. It was used on 65 of our patients; 24 showed a blood volume reduction of more than 600 c.c.

In the light of all the abovementioned studies, we have been able to correct deficiencies preoperatively and prevent complications as far as this was feasible. Pulmonary insufficiency was treated by respiratory exercises under the supervision of a trained physiotherapist. Patients were taught how to breathe and cough. Emphysematous patients were given positive pressure and aminophyllin, which is mainly helpful when there is an elevation of the venous pressure. Bronchodilators like Vaponefrin given in aerosol may be indicated in obstructive endobronchial lesions. Blood volume was preoperatively restored to its normal value.

AT OPERATION

With a better knowledge of the patient's condition and correction of obvious deficiencies, anæsthesia can be more safely begun. During the operative period, the anæsthetist comes up against the problem of anoxia. Anæsthetic agents are a matter of choice. On the other hand, adequate oxygenation of the patient is imperative. We have found that the prone position on the operation table seems to afford better ventilation than the lateral position, but this isolated measure would be inadequate. Endotracheal or endobronchial intubation permits one to deliver oxygen directly into the tracheobronchial tree under well controlled conditions. Oxygen can be given under positive pressure and this may prove very helpful if cardiac arrest occurs. Paradoxical breathing and mediastinal flutter are easily controlled. Free airways are at all times available; secretions can be quickly removed. This is very important when dealing with tuberculous patients where bronchogenic spread may occur. For the surgeon who likes to operate with the patient in the lateral position, we favour the use of the Carlens double lumen catheter. This tube completely separates the two lungs. It prevents flooding of the dependent good lung by secretions coming down from the diseased lung. It permits separate aspiration and inflation of each lung. In the prone position, there is good postural drainage of secretions, which must come down the trachea as soon as they leave the respective lung. A simple endotracheal tube permits good oxygenation without danger of spread. Yet the Carlens double lumen catheter may be helpful in the prone position. The bronchus to be sutured can be completely isolated from the tracheobronchial tree, thus enabling the surgeon to close the bronchial stump under better conditions.

Very few of our patients showed respiratory acidosis. Preoperative and endoperative CO_2 combining power determinations revealed similar figures. There was an increase of 20 volumes per cent in 3.1% of our cases and of 10% in 12% of this series. In only one instance, we found a blood pH of 7.3 at the end of the operation. Arterial oxygen saturation has been consistently normal. During the operation, blood loss is measured by the weighing of sponges and blood is replaced accordingly. This method has appeared satisfactory to us. Postoperative blood volume determinations were closely correlated with the preoperative findings.

Thoracic operations take place in cardiopulmonary zones which contain the most sensitive reflexes of the body. Difficulties arising from vago-vagal reflexes are either of pulmonary or cardiovascular origin. They include bronchospasm with reduction of tidal air, apnœa, A-V block, bradycardia, hypotension, arrhythmia, tachy-arrhythmia, and cardiac asystole. They are more likely to occur in the presence of respiratory acidosis, and their prevention demands the following measures. Intubation must be performed after good topical anæsthesia of the vocal cords and with the patient in a fairly deep plane of general anæsthesia. Spreading of ribs stretches intercostal nerves and may induce the abovementioned difficulties. We routinely block the intercostal nerves as soon as the muscles of the chest wall have been sectioned; we use long-acting agents that may benefit the patient in reducing pain postoperatively. Reflexes due to traction on the pulmonary hilum may be reduced by infiltration of the vagus nerve with procaine or by the intravenous injection of atropine. Reflexes due to pericardial manipulation may be minimized by the intrapericardial injection of procaine. Cardiac arrest is the ultimate effect of anoxia and marked reflex stimulation. If it occurs, the anæsthetist should immediately seek close co-operation with the surgeon and the surgical team, and have the surgeon immediately perform cardiac massage to maintain adequate circulation. The anæsthetist gives oxygen under positive pressure. Intracardiac use of epinephrine may sometimes be helpful.

If ventricular fibrillation occurs, electric defibrillation should be performed. We have had 12 cases of cardiac arrest. They were all treated by oxygen under positive pressure, cardiac massage and epinephrine intracardially. Six patients were successfully treated; the other six did not recover cardiac activity and died.

After Operation

During the immediate postoperative period, the anæsthetist is mainly concerned with removal of retained secretions and with the prevention of atelectasis. When the patient leaves the operating room, his tracheo-bronchial tree should be completely free of secretions, and this freedom must be maintained throughout the postoperative course. Accumulation of secretions interferes with oxygenation by bronchial plugging and often leads to atelectasis, pneumonitis or both. Postoperative excessive formation of secretions can be avoided during the anæsthetic period itself by gentle handling of the tracheobronchial tree and by intermittent inflation of the operated lung. We advocate the use of less depressive sedatives like Demerol, Levo-dromoran, and Largactil. The patient must be encouraged to cough and breathe deeply. Aerosol treatment may be helpful in mobilizing secretions. The patient's position is frequently changed. Intercostal nerve block with a long-acting agent is routinely performed, and alcoholic solutions may be given intravenously. According to Dr. Mary Karp of the Wesley Memorial Hospital, Chicago, the need for narcotics is reduced 30 to 50%; we tend to agree with Dr. Karp's opinion. If these measures fail to prevent retention of secretions or atelectasis, tracheo-bronchial aspiration must be immediately performed. Transnasal aspiration may be tried. Broncho-aspiration is often needed, and tracheotomy sometimes indicated.

Right heart failure sometimes occurs postoperatively. This is to be expected in borderline respiratory cases and in the aged. The anæsthetist must be well aware of this complication. The slightest doubt demands the help of a cardiologist.

Summary

We have stressed the definite importance of preoperative evaluation of the patient in thoracic operations. We have also described methods of prevention and treatment of the more serious complications. Finally, extensive investigation and survey have been possible in

53 consecutive cases recently operated on. In this group of patients, we have had no death and no serious cardio-pulmonary disturbances.

We strongly feel that the great majority of complications can be prevented by a better knowledge of the patient's condition and by proper anæsthetic techniques.

Note.—In addition to the abovementioned thoracic surgical cases, the authors have 75 thoracic cases operated on in different hospitals in Quebec City, in which the cardio-pulmonary disturbances mentioned in this paper were also observed.

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SERUM AMYLASE STUDIES IN SURGICAL PATIENTS*

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THIS INVESTIGATION was undertaken to determine the clinical reliability of serum amylase estimations. It was felt that if serum amylase levels were studied in a series of acute and chronic surgical conditions, both preoperatively and postoperatively, the value of the test in confirming a diagnosis of acute pancreatic disease would be increased. Overconfidence in the significance of serum amylase estimations in the past has occasionally led to pitfalls in diagnosis.

This is illustrated by the case described in Malinowski's review[1] in which treatment for pancreatitis was instituted on the finding of a high serum amylase value and the autopsy demonstrated a perforated duodenal ulcer. Musgrove[2] similarly described three patients with perforation of the gastrointestinal tract and peritonitis associated with elevated serum amylase values. We have observed similar cases and agree that they may be explained by the absorption of pancreatic juices from the peritoneal cavity.

Our study was carried out on a series of patients suffering from a wide range of abdominal conditions, in order to assess more correctly the significance of serum amylase estimations and hence to make it possible to avoid errors of the type described above.

In this series we have used the micromethod of Teller[3] which requires only 0.4 ml. of serum. The reducing substances produced in 30 minutes at 37° C. from starch are determined by Nelson's technique[4] on a Coleman spectrophotometer at a wave length of 660 millimicrons. The error of this method as used by us was ± 2.8% as average variation in duplicate samples.

The normal range of serum amylase was determined by taking specimens from 250 adults who either were in good health or were hospital patients not suffering from any systemic disease. These findings are illustrated in Fig. 1.

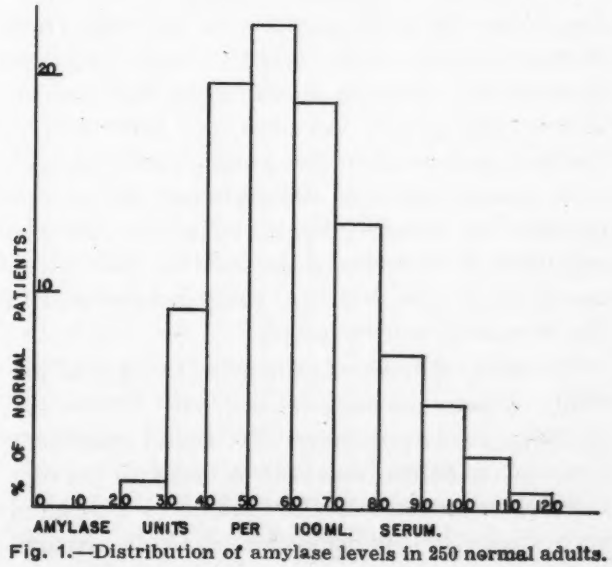

Fig. 1.—Distribution of amylase levels in 250 normal adults.

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The mean of the normal amylase values is 60.1 ± 1.2 units per 100 ml. of serum, with a standard deviation of 19.0 units. By use of the statistical device of ± two standard deviations, the normal range of the enzyme is found to lie between 22 and 98 units. Hence values of serum amylase below 20 units or above 100 units may be considered abnormal (3.2% of our results). Our range of values for the enzyme is appreciably lower than the findings of Somogyi (60-180 units).[5] This discrepancy may be due in part to the fact that enzyme activity was measured at 37° C. instead of 40° C. In addition, in our colorimetric technique, the solution of starch (B.D.H. Analar grade) gave 25-40 mgm. % of reducing substances which are not measured in the iodometric determination. There were no differences in serum amylase levels associated with age or sex.

Our findings agree with those of Somogyi[5] that amylase values are stable for the same person from day to day. In 28 patients amylase levels were determined on two or more occasions. The mean variation was 10%, with a range of 0-30%. This would indicate that variations in enzyme levels in consecutive determinations are significant. The only exception to these figures occurred in a patient with bronchogenic carcinoma, where two determinations yielded values of 23 and 148 units. A bronchoscopic examination had intervened, however, between the two tests.

SERUM AMYLASE LEVELS IN PATIENTS WITH DISEASE

A few slightly elevated values for serum amylase were observed in patients suffering from burns, severe crush injuries, and prostatic hypertrophy. The mean value for this miscellaneous group was 145 units per 100 c.c. The test was performed on five patients with mumps, with a mean value of 306 units per 100 c.c. Although this latter is by no means a new observation, it is included to indicate the extent to which enzyme response could be detected in the disease by our technique.

We were interested primarily in surgical patients. Serum amylase levels were determined in 300 patients preoperatively. Blood specimens were taken before sedation in order to prevent the rise in amylase levels, sometimes associated with spasm of the sphincter of Oddi, particularly where morphine has been used. In some patients one or more postoperative estimations of serum amylase were carried out. We found that surgical intervention invariably produced no significant modification of the preoperative enzyme values.

Our chief interest in amylase studies was the correlation of the amylase levels with the clinical findings in cases of acute pancreatitis. Fourteen examples of this disease are summarized in Table I.

TABLE I.

CASES OF ACUTE PANCREATITIS

Case number	*Serum amylase (units %)*	*Comments*
1	400 90 33	At operation, chronic cholecystitis and lithiasis with pancreatic œdema; values 2, 3, and 5 days after onset of symptoms.
2	390 73	Typical symptoms, conservative treatment; values on 1st and 3rd days.
3	773 155 50	Typical symptoms, conservative treatment; values 1, 6, 15 days after onset.
4	598 118	At operation, associated acute cholecystitis; values on 3rd and 5th days.
5	133	Subsiding pancreatitis on the 5th day.
6	200	Subacute pancreatitis associated with mumps; value on 5th day after onset.
7	230	3rd postoperative day after cholecystectomy.
8	2,670	Typical symptoms, conservative treatment; value on admission.
9	425 150	Typical symptoms, conservative treatment; values on 2nd and 4th day after onset.
10	225 100	Typical symptoms, conservative treatment; values on 2nd and 3rd days.
11	425	At operation, pancreatic œdema associated with chronic cholecystitis; value on 3rd day.
12	560	Typical symptoms, conservative treatment.
13	1,650	Typical symptoms, conservative treatment; value on admission.
14	1,575	Typical symptoms, conservative treatment; value on 2nd day after onset.

It may be observed that all amylase values at first estimations were above normal, ranging from 133 to 2,670 units. The transient nature of the amylase elevation in acute pancreatitis will be noted. The enzyme level may return to normal in a period of one to several days after the acute attack.

Of eight patients with chronic pancreatitis, two with acute pain had values as high as 220 and 535 units, while the others were in the normal range.

Seven patients with carcinoma of the pancreatic head were studied. In four patients normal values for serum amylase were obtained. One had the amylase level slightly elevated to 123 units, while two others had the abnormally high values of 268 and 478 units. In five patients with carcinomas involving the tail and/or body of the pancreas, the amylase values were in the normal range.

In two patients with ulcers penetrating into the pancreas, elevated serum amylase values of 256 and 268 units were demonstrated. In all other patients, in whom a chronic penetrating duodenal ulcer was found at operation, the preoperative amylase level was normal.

Normal enzyme levels were observed in 50 patients with acute appendicitis, seven patients with acute cholecystitis, and patients with miscellaneous acute abdominal conditions such as ectopic pregnancy, strangulated viscera, bile peritonitis, and abdominal gunshot wound.

In malignant disease, amylase values were normal whether the primary tumour was intra-abdominal (33 patients) or extra-abdominal (34 patients). Presence or absence of metastases had no effect on our estimations. In four patients with papillary carcinoma of the colon, slightly elevated or borderline results were obtained. A further study of this problem is under way.

Mean values were not significantly altered in 27 patients with chronic cholecystitis, 30 patients with peptic ulcers, 8 of whom had massive hæmorrhage, or 10 patients with intestinal obstruction.

In general or localized infections, the mean amylase values were lowered, although not significantly, whether the infections were intra-abdominal (15 patients) or extra-abdominal (19 patients). An insignificant rise of the mean amylase values was obtained in 13 patients with arthritis and osteomyelitis.

Elevated levels were observed in two patients with intestinal obstruction: 355 units in a child with strangulation of the small bowel and 205 units in an adult with an obstructed gastroenterostomy. Normal readings, however, were obtained in all other patients with intestinal obstruction, while one patient in a terminal state yielded an abnormally low result of 15 units.

A 50-year-old housewife was admitted to hospital on January 11, 1954, complaining of epigastric pain and vomiting of several days' duration. Serum amylase was markedly elevated to 270 (Teller); 1160 (Somogyi). On her third hospital day she began to vomit brownish fluid and was in shock. The attending physician withheld operation and she died 36 hours later. Autopsy revealed a large chronic pyloric ulcer with slow leak and generalized peritonitis but no evidence of pancreatic disease. This is mute evidence that we must not only originally appraise the abdominal emergency carefully but also re-examine and re-evaluate each case frequently if we are to avoid such errors in diagnosis.

SUMMARY

1. This study was undertaken to determine, if possible, the reliability of the serum amylase test in diagnosis of acute abdominal conditions, particularly pancreatitis.

2. The range of serum amylase levels for adults was established by means of samples taken from 250 healthy subjects, using the Teller microtechnique.

3. Enzyme levels were determined in 300 surgical patients, preoperatively and postoperatively.

4. Abnormally high levels were observed in all of 14 patients with acute pancreatitis. The transient nature of the elevation was stressed.

5. Elevated values were noted in patients suffering from chronic pancreatitis when pain was present, some patients with carcinoma of the head of the pancreas, and penetrating duodenal ulcer, two patients with bowel obstruction and one patient with a perforated duodenal ulcer.

6. Normal values were found in patients with intra-abdominal and extra-abdominal infections, peptic ulcer, incomplete bowel obstruction and carcinoma other than that involving the head of the pancreas.

7. Although this study of serum amylase activity has made us feel that the test is a defendable one, we all realize that no laboratory test makes a diagnosis; there are certain abdominal emergencies in which the serum amylase value will be high, and which may so closely resemble acute pancreatitis that the differential diagnosis cannot be made with certainty. Awareness of the entity, prompt serum amylase studies and careful clinical evaluation will differentiate acute pancreatitis from other acute abdominal conditions.

Canad. M. A. J.
May 15, 1955, vol. 72

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TRACHEOTOMY IN SECRETIONAL HYPOXIA

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MY SUBJECT concerns the more recent aspects of tracheotomy in relation to secretory obstruction. The increase in the indications for this operation is largely due to the fact that it is now commonly used in the treatment of bulbar poliomyelitis.

Historically, tracheotomy was first performed by Asclepiades in the year 124 B.C.[1] for laryngeal obstruction, which has been the main indication for tracheotomy throughout the years.

Numerous authors have shown that hypoxia for from three to five minutes can cause irreversible changes in neural tissue. Our goal, therefore, is to prevent the hypoxic state or correct it as soon as it develops. Within the last decade tracheotomy has been used in the treatment of secretory obstruction causing hypoxia. Secretions enter the tracheobronchial tree, partially blocking it, preventing air from reaching the alveoli, with resulting hypoxia. This occurs only in patients who cannot clear their own secretions. The first essential in asphyxial states is a clear airway to allow absorption of oxygen, but even more important is the elimination of carbon dioxide. There is some evidence to show that carbon dioxide accumulation is responsible for dyspnœa and mental depression, restlessness, disorientation and coma, rise and then later fall of blood pressure, vasomotor failure and circulatory collapse.[2] All of the above have also been credited as symptoms of bulbar poliomyelitis.

The symptoms of hypoxia must be kept in mind if one is to treat this condition satisfactorily. The earliest symptoms are usually mental, the most common being restlessness. It is important because the unwary are tempted to treat it with sedation, and this may be followed by complete respiratory collapse. Other symptoms are depression, confusion, disorientation, combativeness, lethargy, and finally coma. Cyanosis and vasomotor collapse are frequently late signs of hypoxia, and we must recognize the condition before this develops if we are to institute successful therapy. We must remember that the tracheotomy is only a means to an end. It is a means whereby we can safely clear the patient's tracheobronchial tree of secretions by use of catheter suction.

Here, at the Vancouver General Hospital, we do practically all our tracheotomies under general anæsthesia, as we feel that it is safer, and we have more control over the patient's airway. We feel that atropine in these cases is contraindicated as it tends to thicken the secretions and make their removal more difficult. Usually Pentothal and Anectine are used as anæsthetic agents, and an endotracheal tube is inserted. A catheter is passed down the tube and preliminary tracheobronchial suction is done prior to the tracheotomy.

A high tracheotomy is done, usually through the second and third tracheal rings—a small button of tissue being removed from the rings to facilitate insertion of the tracheotomy tube and prevent pressure on the cartilaginous ring margins. One or two sutures are used to close the wound partially as we feel that to leave the wound open helps to prevent emphysema.

Postoperative suctioning of the chest to keep the airway clear is the most important thing that can be done, and it must be done as often as is necessary. It is also important to keep the inhaled air humidified, as this helps to prevent crusting of the secretions in the trachea. At first we use an oxygen catheter directly into the tracheotomy tube. The oxygen is humidified by Alevaire vapour (a commercial detergent) which we find eases the problem of increasing the humidity of inhaled air or oxygen.

The complications of tracheotomy are few, and in our experience the fatal complications are rare. We feel therefore that tracheotomy is not a hazardous procedure. Bilateral pneumothorax is a rare complication but it must be recognized if the patient's life is to be saved, and it is advisable to have a chest radiograph after the tracheotomy is done. In our series of cases we have not seen this complication. Mediastinal emphysema is another complication. This occurs only in a struggling patient. Two of our fatal poliomyelitis cases, in which a tracheotomy had been done, showed mediastinal emphysema at the time of autopsy. Chest infection is a complication which has been fairly common in our tracheotomized poliomyelitis patients. Antibiotics have certainly helped to keep this under control. Crusting of the secretions in the tracheobronchial tree is a complication occurring when humidification is inadequate. The patient's air entry is diminished and the suction catheter cannot be passed very far beyond the end of the tracheotomy tube. We remove the tracheotomy tube and pass a bronchoscope through the tracheotomy incision and remove the crusts with forceps. We have done this in several cases, without mortality. Atelectasis is a fairly common complication in the tracheotomized poliomyelitis patient with respiratory paralysis. Adequate suctioning usually prevents this, but with some superimposed infection it can occur. Positioning and shaking the patient helps to move the secretions. We have also used the "coughing machine" a great deal, with excellent results in the treatment of atelectasis. It is simply a tank-type vacuum cleaner fitted with an attachment which fits into one of the ports on a respirator. The negative intra-tank pressure is increased to about 50 mm. of water and then suddenly reduced to zero or even a positive pressure. The patient coughs. This is done several times, and a suction catheter is passed via the tracheotomy tube and the secretions are removed from the tracheobronchial tree.

POLIOMYELITIS

I would like to discuss some of the hypoxic conditions in which tracheotomy has been used with gratifying results. Tracheotomy for secretional hypoxia was first used in a large series of cases in bulbar poliomyelitis by the Minnesota group under Priest, Boies and Goltz,[3] who published a report in 1947 on their devastating 1946 epidemic of poliomyelitis. They had 1,830 cases, of which 400 were "bulbar" and 75 had tracheotomies done. Twenty-nine survived—that is, a mortality rate of 61%. Since then about 30 to 40 papers on tracheotomy in bulbar poliomyelitis have been published, with varying opinions as to its efficacy. However, the majority of the authors who have used it feel that it has saved the lives of many poliomyelitis patients.

The following indications for tracheotomy are applicable to secretional hypoxic states: (1) secretions in the upper airway with signs of hypoxia in spite of the administration of oxygen, postural drainage and aspiration; (2) unconsciousness or marked restlessness in a poliomyelitis patient not responding to other treatment in a few minutes; (3) signs of hypoxia in a respirator patient even if he has a pure spinal type of poliomyelitis; (4) rapidly progressive signs of bulbar poliomyelitis; and (5) bilateral paralysis or spasm of the vocal cords.

Tracheotomy, when indicated, should be done early and not as a last resort when the pathological changes may be irreversible.

At the Vancouver General Hospital in the last five years we have done tracheotomies on 84 poliomyelitis patients, and 18 of these died, which is a mortality rate of 21%. We feel that 30 to 40% of these patients would certainly have died if a tracheotomy had not been done. Bulbar poliomyelitis patients are poor risks for transport by air. If they must be transported in the acute phase of the disease, and if the patients cannot clear their own secretions, we insist on a tracheotomy prior to air transportation, and on expert attendance during transportation.

Galloway,[4] one of the outstanding authorities on this subject, stated recently; "On studying our own records, I am shocked to find that of nine patients with bulbar symptoms who were placed in a respirator without tracheotomy at any time, only one survived."

Priest[5] and Orton[6] have reported several cases of botulism successfully treated with tracheotomy and respirator. The similarity of botulism and bulbar poliomyelitis is very striking.

OTHER CONDITIONS

In severe barbiturate poisoning there is profound depression with loss of cough reflex and eventually cessation of respiration. Two cases of tracheotomy in barbiturate poisoning were reported by Lewy and Sibbitt.[7] The respirator is

Canad. M. A. J.
May 15, 1955, vol. 72

used if indicated. If the cough and gag reflex have not returned in from eight to 12 hours, a tracheotomy should be done. In the past year we have had two of these cases treated with tracheotomy, and both recovered completely.

TABLE I.

TRACHEOTOMY FOR SECRETIONAL OBSTRUCTION CAUSING HYPOXIA. (VANCOUVER GENERAL HOSPITAL, 1946 - 53).

	No.	*Deaths*
Poliomyelitis	84	18
Guillain-Barré syndrome	5	0
Severe head injuries	4	2
Fat embolism	1	0
Acoustic neuroma	1	1
Fracture cervical spine	2	0
Benadryl poisoning	1	1
Atelectasis following resection of maxilla	1	1
Pulmonary œdema	1	1
Cerebral vascular accident	2	1
Postgastrectomy atelectasis	1	0
Phenobarbitone poisoning	2	0
	105	25

Mortality rate—23.8%

Echols *et al.*[8] reported on tracheotomy in the management of severe head injuries. "It is generally agreed that an almost perfect airway is of supreme importance in patients unconscious from head injuries, but use of the endotracheal tube and tracheotomy for this purpose has been neglected." Use of the endotracheal tube is indicated when the respiratory difficulty is likely to be resolved in eight to 12 hours. They reported 15 patients who had tracheotomies after severe head injuries, eight of whom required neurosurgical procedures—9 patients survived. In our series, we have treated four of these cases, with two deaths.

In 1949, Turner and Galloway[9] reported that tetanus under control by curare presented almost the same picture as bulbar poliomyelitis, and responded to the same measures. With elimination of the primary focus, this disease usually runs a self-limited course of from eight to 12 days. The common cause of death in these cases is respiratory.

Atkins[10] has shown the value of tracheotomy in postoperative or debilitated patients, especially after operations involving the mouth, pharynx or neck. The cough reflex in these patients is too weak to be effective. These older patients frequently die of so-called "hypostatic pneumonia." When the patient cannot cough effectively and has much secretion, a tracheotomy is the safest and most practical treatment procedure. We had one such case in our series.

Another disease very similar to poliomyelitis is known by various names, the commonest of which is Guillain-Barré syndrome, or acute infectious polyneuronitis. This disease affects the motor system as does poliomyelitis, but there are also sensory disturbances. It frequently presents the same respiratory problem and the treatment, therefore, is the same. It differs from poliomyelitis in that, if one is able to bring the patient safely through the acute phase of the disease, recovery is complete, there being no sequelæ. I have been able to find in the literature only one such case treated by tracheotomy. This was reported by Fitz-Hugh and Morgan.[11] We have treated five such patients in our series, and all have recovered completely. Three of the five were quadriplegic and in a respirator, and we feel these three would certainly have died had a tracheotomy not been done.

SUMMARY

The basis for tracheotomy in the treatment of secretional hypoxic states has been presented, and an effort made to show that it is a practical and effective procedure in the treatment of these conditions.

Even though one may feel that the patient's hypoxic state is due to his severe infection rather than secretional obstruction, it is still safer to assume that the cause is mechanical, and to perform a tracheotomy. For maximum effectiveness the decision must be made and acted upon as early as possible.

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Case Reports

HÆMORRHAGIC DIATHESIS ATTRIBUTED TO "WARFARIN" POISONING

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WARFARIN, or 3-(α-acetonylbenzyl)-4-hydroxycoumarin, is a dicoumarol-like substance with a prolonged and hence cumulative action. It has been used in clinical medicine because, in addition to being effective orally, it can be given parenterally.[1] However, this substance has been mainly used as a rodenticide, being marketed under a variety of trade names.[2] It is used for poisoning bait. The pests eat the bait on several successive days, develop a defective clotting mechanism, and die of hæmorrhage. It is hoped that domestic animals and children inadvertently eating some of the bait will have only a single exposure, which is unlikely to produce untoward symptoms.

One human case of Warfarin poisoning has been reported, where the substance was knowingly ingested in an unsuccessful suicide attempt.[3] In Korea, poisoned bait was eaten by a Korean family and several members died from hæmorrhage.[4]

In the following case, circumstantial evidence suggests that accidental Warfarin poisoning was responsible for a hæmorrhagic diathesis.

Mrs. E.W., a farmer's wife, was born in 1911. She was seen in April 1954 complaining of hæmaturia and easy bruising. There was no family history of any bleeding tendency, and she had been well most of her life. In 1931 a tonsillectomy was done without mishap, because of recurrent sore throats. An emergency appendectomy in 1933 was uneventful. Her pregnancies were normal, and deliveries without incident. She had never had jaundice, nor did she ever have bouts of diarrhœa or loose stools. Following the delivery of her youngest child in 1943, she noticed that her menstrual periods, while regular, were more profuse. This complaint gradually became more marked and she was told that she was anæmic because of this, and was placed on iron medication intermittently. In November 1952, she was admitted to hospital because of continued menorrhagia. Examination at this time revealed nothing remarkable except for pallor, and the presence of a large uterus. Her hæmoglobin value was recorded as 58% (9 gm.), red cell count as 4.0 million per c.mm. Her prothrombin time was 13.5 seconds (100%). She was given four blood transfusions and a hysterectomy was done; the pathological diagnosis was adenomyosis of uterus. She had no postoperative complications and was discharged with a hæmoglobin value of 81% (12.6 gm). Her usual weight was 105 lb.; following operation it was 97 lb. and remained at this level.

She was well during the winter of 1953 except for an intermittent eczematous eruption of her hands, attributed to some undetermined contact allergen. In May 1953, she noticed that she was bruising easily and at this time she began to pass grossly bloody urine. She was admitted to her local hospital and was treated with vitamin K injections. Her bleeding ceased, and she was discharged. She remained well for the remainder of the year.

In mid-April 1954, she had a recurrence of easy bruising and hæmaturia. Nothing further was uncovered in history and she denied taking any medicines and any exposure to chemical agents. On examination at this time it was noted that she was a thin woman with scattered ecchymoses on her arms and legs. A single spider nævus was present above her left orbit. No petechiæ were seen on skin or mucus membranes. She had no palpable lymph nodes; spleen and liver were not palpable. There was no bone tenderness. Blood pressure was 120/180. A Rumpel-Leede test for increased capillary fragility was negative.

Bleeding and clotting times were normal. Clot retraction was normal. Platelet count was 240,000 per c.mm. and platelets were normal in appearance. Hæmoglobin value was 90% (14 gm.), white cell count 7,700, with a normal differential. Blood urea nitrogen was 18 mgm. %; serum protein 6.7 g. % with albumin 5.0 g. %, globulins 1.7 g. %, gamma globulins 0.6 g. %. No cryoglobulins were found. Sedimentation rate (Westergren) was 13 mm. in one hour. Urinalysis showed only an occasional red cell. Thymol turbidity was 4 units; thymol flocculation was negative; cephalin cholesterol flocculation was one-plus in 24 hours.

Her prothrombin time, measured by Quick's one-stage method, was 18 seconds, or 50% of normal. The following day it was 15 seconds, or 70% of normal, and two days later it was 13 seconds or 100%. A prothrombin consumption test done at this time was normal, as over 85% of the prothrombin was consumed.

Intravenous pyelograms were normal. Inquiry again with regard to salicylate or other chemical ingestion or exposure was negative. She was sent home after spontaneous improvement without the luxury of accurate diagnosis.

On May 19, 1954, the patient was admitted to hospital as an emergency. She complained of faintness, ecchymoses, black tarry stools and hæmaturia. On admission her hæmoglobin value was 58% (9 gm. %) and her prothrombin time was over 2 minutes, or less than 10%. She was given two bottles of stored blood and 1 c.c. of synthetic vitamin K containing 15 mgm., intramuscularly. She was watched carefully for signs of shock, but because of rapid improvement no further transfusions were given, although vitamin K injection was continued daily. Her progress continued to be satisfactory; all bleeding stopped and her prothrombin time returned to normal by May 25. In two weeks she had apparently recovered completely and was discharged.

Additional tests were run on a sample of blood taken on May 19, 1954, just after the patient had received her first bottle of blood. These tests consisted of making mixtures of the patient's plasma with various other plasma and sera and comparing the prothrombin times of these mixtures with controls.

The mixture of patient's plasma and normal plasma (Table I) gave a prothrombin time somewhat better than a mixture of normal plasma and inert saline. This was interpreted as indicating that there were no potent inhibitors in the plasma of the patient, and that it did contain factors contributing to the clotting.

Canad. M. A. J.
May 15, 1955, vol. 72

TABLE I.

Patient's plasma	*Normal plasma*	*Normal serum*	*Normal saline*	*Dicoumarol plasma*	*Prothrombin time*
0.1 c.c.	0.1 c.c.	—	—	—	15 sec.
—	0.1 c.c.	—	0.1 c.c.	—	18 sec.
0.1 c.c.	—	0.1 c.c.	—	—	30 sec.
0.1 c.c.	—	—	—	0.1 c.c.	60 sec.
—	—	—	—	0.2 c.c.	30 sec.
—	—	—	0.1 c.c.	0.1 c.c.	60 sec.

Normal serum was mixed in equal quantities with the patient's plasma. This serum had no demonstrable free thrombin. Serum contains very little prothrombin or accelerator globulin, but does contain factor VII. The serum was able to restore the patient's prothrombin time to near normal. This suggests that the defect in the patient's plasma was largely in factor VII, although probably small defects in prothrombin and accelerator globulin were also present.

The mixture of patient's plasma with plasma from a patient on dicoumarol gave a prothrombin time much the same as mixing the dicoumarol plasma with saline. This suggests that the same defect was present in both of these plasmas.

It would seem, therefore, that this patient had a factor VII defect that was corrected rather rapidly by a small amount of blood and by inadequate doses of synthetic vitamin K rather than fat-soluble K. The whole response was so similar to that which follows discontinuation of a dicoumarol-like drug that this possibility was again questioned. It was then discovered that there had been a large number of rats about the farm during the past two years and that Warfarin had been used in order to control them. The patient mixed up all batches of bait herself, and remarked that each of her hæmorrhagic episodes had followed a period when she was mixing up successive batches of poisoned bait.

How did the drug get into the patient? She is certain that there was no chance of her having ingested any of it. She did remark that there was quite a bit of the powder in the air when she was mixing it, and that it made her sneeze. Possibly she might have inhaled sufficient to produce the effect. However, the powder that she was using was 5% Warfarin in starch, and a considerable amount would have to be inhaled. A single dose of 50 mgm. of Warfarin by injection can produce significant hypoprothrombinæmia.[1]

The possibility of cutaneous absorption cannot be dismissed. It would be likely if the patient had had her eczematous eruption during this time, but the rash was not present during her last two bleeding episodes.

In any case, it would seem likely that this woman was unusually sensitive to the action of the drug. It was proposed to test this hypothesis by observing the effect on this patient's prothrombin time of a single, small dose of dicoumarol, but the patient was understandably reluctant to submit to this test. She was advised to discontinue the use of this poison, and to date she has remained well.

SUMMARY

A case is reported of a hæmorrhagic diathesis associated with hypoprothrombinæmia as detected by the one-stage Quick method, but probably due to diminished factor VII. Circumstantially, this was attributed to exposure to a pesticide, Warfarin.

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CARCINOID TUMOUR OF THE RECTUM*

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CARCINOID TUMOURS of the rectum are not common. In 1942, Stout[1] found 14 cases reported in the world literature and added six of his own. By the middle of 1953 a total of 83 cases had been reported (Haynes *et al.*[2]). This great increase in the last 10 years indicates an increasing awareness of the condition.

Carcinoid tumours may occur in all portions of the intestinal tract, including stomach, duodenum, gallbladder, jejunum and Meckel's diverticulum. They are usually thought to arise from the cells of Kultschitzky, in the crypts of Lieberkühn. These cells are found throughout the intestinal tract, but are most common in the ileocæcal area and this is where most carcinoids

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are found. The origin of these cells has been disputed, opinion being divided over their origin from ectodermal or endodermal sources. They have some resemblance to adrenal tissue and are thought to be part of the general chromaffin system.

The cells usually have an affinity for silver stains and carcinoids are sometimes called argentaffinomas. However, not all carcinoids take silver stains and this is particularly true of those occurring in the rectum. Because of this, the term carcinoid, in spite of objections by some investigators, is probably to be preferred. The term was introduced by Oberndorfer[3] in 1907 because the lesions looked like carcinomas but seemed to be benign. If we add the modern knowledge that any carcinoid can be potentially malignant, the name applied matters little.

The malignant potentiality of carcinoids is extremely variable. Those occurring in the appendix (the commonest site) very rarely metastasize. Anywhere else in the tract carcinoids are clinically much more malignant. Pearson and Fitzgerald[4] reported 38% metastases in extra-appendiceal carcinoids. Haynes *et al.*[2] state that there is a 12% metastatic rate for rectal carcinoids. The reason for this variation is unknown. It has been postulated that the malignancy might be related to the presence or absence of silver-staining granules. It seems certain that appendiceal carcinoids cause symptoms very early and are removed before spread occurs. In the rectum many have been discovered early because of the increasing routine use of proctosigmoidoscopic examination. Even though metastases occur, they may grow slowly and these cases run a longer course than in most other malignant diseases.

CASE REPORT

A 52-year-old white male was admitted to the St. Thomas Memorial Hospital on March 15, 1952, because of sudden, severe abdominal pain. He had a right indirect inguinal hernia in which was pinched a piece of bowel or omentum. When he had been given morphine and put to bed, the hernia reduced and the pain disappeared.

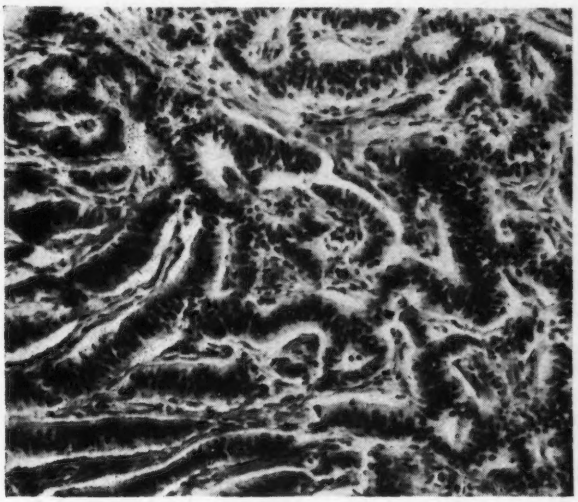

Fig. 1

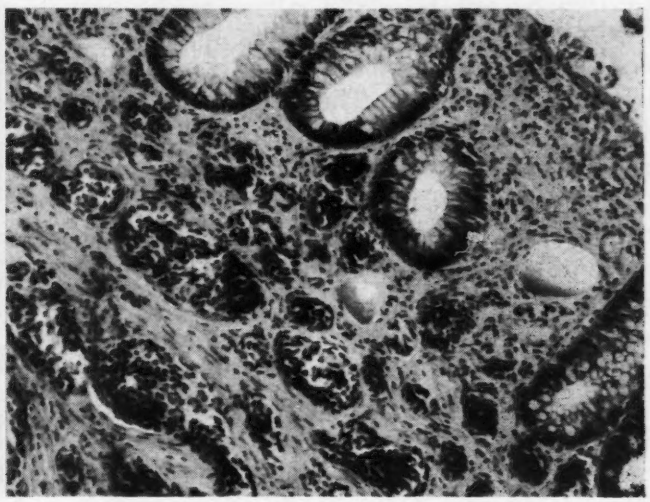

Fig. 2

Fig. 1.—Typical area of tumour showing "festooned" ribbons of cells characteristic of rectal carcinoids. x325. Fig. 2.—Showing focus of tumour cells infiltrating the mucosa. Many of the cells appear necrotic. Elsewhere, the mucosa remained intact above the tumour. x325.

Because of a history of various digestive aches and pains, which were vague in character, it was decided to investigate the case more thoroughly. Gastrointestinal and gallbladder x-ray examinations were done, with negative results. He was also examined with the sigmoidoscope and a small, sessile polyp was found in the rectum. It was located on the anterior rectal wall about three inches (7.5 cm.) from the anal margin and was about the size of a large match head. A barium enema examination gave negative results. General physical and laboratory examinations revealed nothing more.

The tumour nodule was removed by means of the biopsy forceps, transecting it across the base. The surrounding mucosa appeared perfectly normal and there was no alteration in the lumen of the rectum. The pathologist reported that the specimen consisted of an oval-shaped nodule measuring 1 x 0.9 x 0.8 cm. On section it presented a fleshy, greyish appearance and appeared encapsulated. Microscopically, the section was covered by an intact but thinned mucosa in which the glands were well defined and typical. Within the submucosa was a roughly circumscribed and partially encapsulated nodule of tumour tissue composed of convoluted ribbons, columns, pseudoglands and solid groups of columnar and polygonal cells and supported by fibroblastic tissue. The nuclei were small to moderate in size, stippled and of very uniform staining intensity. Mitotic figures were essentially absent. This lesion was considered to be primary in the rectum and to represent a glandular type of argentaffin or so-called carcinoid tumour (see Figs. 1 and 2).

Canad. M. A. J.
May 15, 1955, vol. 72

Examination in January 1954, almost two years following removal, revealed no signs of recurrence in the rectum and no signs of local or distant metastases. The patient appeared perfectly well.

Most rectal carcinoids are small, submucosal nodules like this one. They are frequently found on the anterior rectal wall (Epps *et al.*[5]) 3 to 10 cm. from the anus. Some rectal carcinoids may be plaque-like and some are pedunculated. Occasionally invasion of the muscularis and serosa has been described and occasionally an annular, constricting type is found. The microscopical description is usually very similar to that outlined above. The age of onset varies from 14 to 71 years (average 44). The lesion occurs somewhat more commonly in women than in men. In most cases, few symptoms related to the tumour have been reported. In the case here reported it was felt that the symptoms were not related to the tumour. Larger carcinoids have caused pain, bleeding and obstruction. Most cases have been discovered as a result of routine examination of the rectum.

The treatment of carcinoids of the rectum varies from local excision to abdomino-perineal resection. In cases of large, invasive carcinoids with or without metastases and with or without annular constriction, treatment is by abdomino-perineal resection. Solitary distant metastatic lesions should, if possible, be excised. Local excision of the usual small submucous polyp appears to be justified as the treatment of choice (Epps *et al.*,[5] Raven[6]). Twenty-nine such cases have been reported up to 1953 with no recurrences as long as 9 years later. The patient should be kept under observation, and if a recurrence is found a radical operation should be carried out. It should not be forgotten that metastases can occur even though the rectal lesion is small. Metastatic spread has been reported to sacral and aortic nodes and to liver, vertebræ, kidney, pancreas, lungs and spleen.

The results of use of radium and x-rays have been inconclusive; this is because even malignant carcinoids run a remarkably chronic course and some patients have lived for years with stationary metastases (Epps *et al.*[5]).

SUMMARY

A case of carcinoid of the rectum is presented. The main points of pathology, symptoms and treatment are outlined. It is emphasized that most carcinoids of the rectum are small polyps producing no symptoms and are best treated by local excision. However, carcinoid of rectum may be large, invasive and obstructive and it must always be remembered that even the small ones may metastasize.

The author would like to thank Dr. C. Wallace, pathologist at the Memorial Hospital, for the pathological examination and report.

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MYASTHENIA GRAVIS NEONATORUM*

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MYASTHENIA GRAVIS is encountered in childhood in three distinct types: (1) acquired myasthenia gravis, differing in no way, except in its rarity, from the disease acquired in adult life; (2) true congenital myasthenia gravis, of which six cases have been reported in the literature, all born to healthy mothers and all with persistent signs; (3) transient myasthenia gravis syndrome of the newborn, of which 15 cases have been reported in the literature, all born to mothers suffering from myasthenia gravis during their pregnancy. Some infants with transient myasthenia are so severely affected that they die shortly after birth from their myasthenia or recover only with Prostigmine (neostigmine) and intensive nursing care. Other infants may have transient myasthenia with signs so mild as to escape detection unless studied with great care. The placentally transmitted substance responsible for the myasthenia in the infant is totally excreted after a period varying from a few days to five weeks, after which the child is free from all symptoms and signs of myasthenia.

In 1951 the author,[1] in association with Dr. H. M. Kidd, reported three cases of transient myasthenia gravis syndrome of the newborn, one of

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them in great detail, and summarized the literature on the six previously recorded cases. Recently Kibrick[2] has made an exhaustive review of the literature to date, which brings the total of true congenital myasthenia cases to six and of transient myasthenia of the newborn to 15. It is interesting to note that more than half these cases have been reported in the past three years.

The object of this report is to record another case of transient myasthenia of the newborn and to draw attention again to the need for detailed careful examination of infants born to mothers with myasthenia gravis.

Mrs. P.E., born in 1919, has had three pregnancies. The first pregnancy produced a normal child. In 1946, in the fourth month of the second pregnancy, she began to see double and became unable to comb her hair. The records show that she was considered psychoneurotic and a diagnosis of myasthenia gravis was not made until 1949. The full-term child born of this second pregnancy (1946, before the mother was known to be myasthenic) was seen by a pædiatrician on the third day of life and described as showing "no evidence of cerebral damage" and on the sixth day of life as "sucking poorly but showing no evidence of cerebral damage." The record states that on the third day of life the infant was sucking poorly, and on the fifth day of life was fed every three hours from a Breck feeder. The mother reports that the child was more than three weeks old before he could take more than an ounce at a feeding.

On October 29, 1954, with her third pregnancy, during which she required her accustomed 90 mgm. of Prostigmine daily, Mrs. P.E. was delivered after a short labour with very mild anæsthesia of a full-term 7-pound girl whose fetal movements had been normally active. Fifteen minutes before delivery the mother was given intramuscular Prostigmine; the child breathed and cried spontaneously and was lively. Four hours later the infant was mildly hypotonic, particularly in the neck region, showed absent rooting reflex, a weak sucking reflex and gag reflex, a poor Moro reflex, a weak cry, and a great excess of mucus in the nasopharynx requiring very frequent suction. These signs became more marked during the next twelve hours, the face became relatively expressionless, and it was obvious that the baby had the myasthenia syndrome. Prostigmine 0.05 to 0.15 mgm. was given as indicated every 4-6 hours, and this produced a dramatic increase in tone of all the involved structures. After four days Prostigmine was given only once a day and on the seventh day was discontinued, at which time the infant was normal except for slight impairment of her general tone. On the fourteenth day of life she was discharged, quite well and taking all her feedings by bottle. A coloured motion picture film showing the dramatic Prostigmine effect had been made on the second day of life.

DISCUSSION

The literature on myasthenia gravis is replete with statements that myasthenic mothers produce normal children. Of the cases reported by the author, among six pregnancies of three myasthenic mothers, four infants were diagnosed as having transient myasthenia of the newborn, one was described as normal, and one (P.E.'s second pregnancy) sucked very poorly for three weeks. One of the author's cases was so severely affected that except for the unusual ability of the pædiatric house physician it could not have survived. The case reported here, were it not for the acumen of the pædiatric intern, might well have escaped diagnosis and been considered a hypotonic infant with excess mucus and poor sucking ability. The author therefore suggests that if the newborn infants of all mothers with myasthenia gravis were carefully studied for the first 24 hours, with detailed and repeated examination of the tonus of the muscles supplied by the cranial nerves, it might be demonstrated that myasthenic mothers do not produce normal children.

SUMMARY

1. A case of transient myasthenia gravis of the newborn is recorded, the fourth reported by the author, the sixteenth in the literature.

2. The statement encountered in all the literature on myasthenia gravis that "myasthenic mothers produce normal children" should be regarded with scepticism.

3. All newborn infants of myasthenic mothers deserve a detailed scrutiny of their muscle tone, particularly in those areas supplied by the cranial nerves.

4. In the newborn the triad of hypotonia, poor sucking ability, and excess mucus in the nasopharynx should cause the attending physician to consider myasthenia gravis in his differential diagnosis.

The Prostigmine used in the treatment of this infant was supplied by Hoffmann-LaRoche Limited.

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THE USE OF THE MEDICAL LIBRARY

There is an old Welsh curse called down on the person who misdirects the weary traveller. This should be amended to include him who gives a wrong reference. The most important part of a paper may be its references and the watchword here should be check, check and then recheck. One of the most aggravating of the librarian's tasks is to seek a reference copied from article to article which is wrong. I know the exhaustion which affects the writer of articles when he comes to the last pages of his work but I would appeal to him to take another day at it to check his references.—A. L. Goodall: *Glasgow M. J.*, 35: 366, 1954.

Canad. M. A. J.
May 15, 1955, vol. 72

Special Article

THE RELATIONSHIP OF DOCTORS AND HOSPITALS

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HIGH AMONG the assets and conveniences of the physicians of today is the modern hospital, well equipped with the advanced facilities for treatment of the sick. The public appreciates the value of good hospitals and has provided for their establishment through private, organizational and government funds. The motivating force behind the demand for hospital construction is the medical profession. Why? Because adequate hospital accommodation for our patients not only means better treatment for the patient but also assures treatment in most favourable circumstances, resulting in an economy of time and greater freedom from anxiety for the attending physician.

Altruism alone does not prompt a doctor, contemplating establishing a practice, to inquire about the hospital facilities of a community. The hardships and inefficiencies of a house-to-house practice, the long vigil at the bedside of a critically ill patient, and the restrictions that are inevitable through distances and lack of trained personnel have little appeal. It is the district served by a good hospital that attracts the members of our profession.

RESPONSIBILITY AND PRIVILEGES

What responsibility has a doctor to the hospital in which he has been accepted as a medical staff member? What are the privileges that he enjoys when those responsibilities are properly discharged?

The medical staff is responsible for the quality of medical care given to the patient, and in conjunction with the administrative authorities should always consider the best interests of the patients.

The care of a patient in a hospital is a cooperative effort. All members of the therapeutic team should place the interest of the patient in the foreground. Personalities, personal ambitions and petty jealousies should not be permitted to cloud the ultimate objective—the best possible care of the patient.

To obtain satisfactory results, any organization or business must be well and thoroughly organized. The hospital is no exception to this axiom. The ultimate responsibility for the operation of a hospital rests with the governing body. This responsibility is not only moral but also legal, as set forth in the Public Hospitals Acts of our various provinces. The basic principles of hospital organization have been drawn up and approved by the Joint Commission on Accreditation of Hospitals and the Canadian Commission on Accreditation of Hospitals. The member organizations of the former commission are the American College of Surgeons, American College of Physicians, American Medical Association, Canadian Medical Association and American Hospital Association. The latter commission is sponsored by the Canadian Medical Association, Association des Médecins de Langue Française du Canada, Royal College of Physicians and Surgeons of Canada, and Canadian Hospital Association. These organizations represent the most experienced groups on this continent dealing with the health problems of our citizens. An accepted principle of hospital organization is that the medical staff shall be self-governing. Sometimes complaints are heard of administrative interference; such assertions overlook the fact that by-laws, rules and regulations, conforming with the best thought of organized medicine and hospital administration, have been adopted by the medical staff and approved by the governing body of the hospital. In those by-laws certain specific action is required of the medical staff. If this responsibility is neglected, the governing body or its executive representative, the hospital administrator, must make every effort to correct the deficiencies. This, without prejudice, should not be interpreted as interference. The custodians of a public trust, as represented in the operation of a hospital, are bound to require that the medical staff discharge its responsibilities in addition to utilizing its privileges.

MEDICAL STAFF ORGANIZATION

To some, proper organization may seem difficult, but many of the problems that appear insurmountable will disappear if there is complete harmony and unity of purpose among the staff members. It is seldom difficult to decide on a chief-of-staff, but an appreciation of his duty to supervise actively and to control the clinical work in the hospital may not be accepted graciously.

A high standard of surgery and the elimination of unnecessary or questionable surgery should be the objective of every hospital. Improvement of quality has been noted in those institutions where a tissue committee actively functions and where strict supervision by the head of the surgical department is thoroughly endorsed and supported.

Frank and free discussion of cases in staff meetings and clinico-pathological conferences will lead to a higher degree of scientific efficiency among staff members. The problem of obtaining good medical records, the responsibility of the physician, is a universal one and more often stems from lack of the habit of recording findings than from the lack of time, so frequently advanced as a reason for inadequate records. Good records are a time-saving factor and avoid

possible error in treatment and diagnosis. They reflect the interest of the staff in promoting scientific medicine and the thoroughness of the clinical investigation. They are essential for a complete review and analysis on presentation of cases at clinical conferences. They are invaluable for future reference. They often have a direct economic value in the completion of claims, both for patient and doctor.

The reluctance of some doctors to ask for a consultation is gradually disappearing. Consultations, apart from the valuable interchange of scientific knowledge between the consulting parties, give to the patient a sense of security and assurance that every consideration is being given to the case. Consultations may also be a protection to the hospital and to the doctor. Therefore, they should always be recorded, and contain sufficient clinical data to justify the diagnosis and warrant the surgical procedure or treatment recommended.

Physicians should assume their responsibilities because they must fully appreciate the inestimable advantages that accrue to the patient through hospital treatment. The comparative ease with which complicated therapeutic measures may be carried out with adequate equipment and trained personnel, and the satisfaction of returning the patient to an active role in the community as quickly as compatible with safety, are self-evident.

The daily association and free exchange of ideas and opinions with others in the profession is a privilege that merits recognition. The educational value of departmental conferences, clinico-pathological sessions and staff meetings is highly regarded by all interested in the progress of medical science and the better care of the patient.

The availability of good medical records for clinical studies furnishes an opportunity for research that cannot be found elsewhere.

If a doctor is associated with a hospital, he is vitally concerned with the reputation and status given that institution by his colleagues in other hospitals and by citizens of the community which he serves. That reputation rests largely with the members of the medical staff and should be zealously guarded by them.

JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

The medical organizations mentioned earlier in this article have set up the Joint Commission on Accreditation of Hospitals. The purposes of that Commission are:

"(a) To conduct an inspection and accreditation programme which will encourage physicians and hospitals of the United States and Canada voluntarily:

1. To apply certain basic principles of organization and administration for efficient care of the patient.

2. To promote high quality of medical and hospital care in all its aspects in order to give patients the greatest benefits that medical science has to offer.

3. To maintain the essential services in the hospital through co-ordinated effort of the organized medical staff and the governing board of the hospital.

(b) To establish standards for hospital operation."

That the leaders in our profession realized the need for hospital boards, medical staffs and hospital administrators to have a source from which help and guidance in organization and operation could be obtained is evidenced by their support of the Joint Commission on Accreditation of Hospitals. The Commission is prepared to give any assistance requested. It has formulated basic standards for accreditation which place responsibility upon the medical staff and the administration. These responsibilities are associated with privileges and advantages that outweigh the obligations.

Hospital administrators are alive to the challenge "to give patients the greatest benefits medical science has to offer." *They cannot do it alone.* We, as physicians, must assume our share of the task, accept self-government, organize effectively and operate in the interest of our patients and of the progress of medical science.

SUMMARY

The following questions, with brief answers, are suggested:

1. Are hospitals essential?
2. Has organization any value?
3. Are the problems encountered in good staff organization insurmountable?
4. What are the doctor's responsibilities to his hospital?
5. Does a conscientious approach to the responsibilities produce better hospital administration and patient treatment?

244 St. George St., Toronto.

INCREASED LABOUR COSTS

The American Blue Cross Commission announces the birth of a child to Mrs. Ann W. Reid, whose own birth was the first ever covered by the Blue Cross Hospital Service plan.

Interesting as this may be as regards the passage of time, there is probably more significance in the changes that have taken place in the intervening period between the two births. The first mother spent ten days in hospital when her child was born, and the total bill was $60.00; this was in December 1933. The second mother, in 1955, was in hospital for her baby about half that time, and her bill was about $115.00.

Canad. M. A. J.
May 15, 1955, vol. 72

Clinical and Laboratory Notes

THE USE OF ACTH AND CORTISONE IN CHILDHOOD ALLERGIES*

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DURING the past few years ACTH and cortisone have been added to our armamentarium for the treatment of the allergic states. This paper will review briefly the use of these drugs in treating allergies in children. For more detail of the literature, the reader is referred to reviews by Cooke[1] and by Brown.[2]

In using these drugs in the allergic state it is essential to remember that they are in no sense curative. They may be used to give the patient symptomatic relief, and on occasion may be used to meet an acute emergency which might otherwise end fatally, but in no case must they be used unless generally accepted anti-allergic care is also instituted, since the latter is the only method of treatment carrying any hope of giving the patient permanent relief.

Asthma.—There are three indications for the use of ACTH and/or cortisone in asthma. (1) They may be used for the treatment of the acute attack, especially status asthmaticus. (2) They may be used for the long-term management of a patient with very severe symptoms, while waiting for the accepted anti-allergic therapy to become effective, in order to tide the patient over this very trying period. (3) They may be used for the rare patient who does not respond to anti-allergic therapy. This latter indication is extremely rare in childhood.

Oral cortisone is preferable for long-term management in a dosage of 12.5 to 25 mgm. at 4-hour intervals five times a day for an infant or small child, and 25 to 37.5 mgm. at 4-hour intervals five times a day for an older child. These are initial doses. As the patient shows improvement the dosage should be gradually reduced, and finally a maintenance dosage just sufficient to keep the patient reasonably comfortable should be used. Frequently this is only 25 to 50 mgm. a day. For the treatment of the acute attack in the hospitalized patient, one may use intramuscular cortisone as a single injection daily of approximately two-thirds of the daily oral dose for that child, or one may use intramuscular ACTH in a dosage of 5 mgm. 6-hourly for an infant or small child, 10 mgm. 6-hourly for an older child. Again the dosage should be decreased as rapidly as possible, consistent with reasonable relief of the patient. For the treatment of status asthmaticus it is preferable to use intravenous ACTH in a dosage of 10 mgm. for an infant or small child, or 15 mgm. for an older child. In either case this should be given in 5% glucose in distilled water over an 8-hour period and may be repeated the next day, and possibly the following day, if the patient has not shown satisfactory recovery.

Many authors have reported the treatment of bronchial asthma with ACTH and cortisone, for example Glaser,[3] Schwartz[4] and Lowell *et al.*[5]

Hay fever.—ACTH or cortisone is rarely required in the treatment of hay fever in children. This disease in children usually responds well to the usual methods of anti-allergic therapy and to the commonly used medications such as the antihistamines, ephedrine and aminophylline compounds. If necessary for the relief of very severe symptoms the drug of choice would be oral cortisone given in the same dosage as for asthma. Schiller and Lowell[6] have reported a series of hay fever cases treated by this method.

Eczema.—There are four indications for the use of ACTH and cortisone in eczema. (1) To control a very severe exacerbation of the disease which is causing a great deal of distress to the patient. Its value in this condition is of a very temporary nature only. (2) To give the patient a reasonable amount of relief while waiting for the orthodox methods of treatment to become effective. In this case it may be used for a period of a few months after treatment is first started. (3) To clear the skin temporarily so that skin testing can be done. This is useful in cases of generalized eruption with no normal skin on which skin testing can be done. It has been shown by Bowman *et al.*[7] and others that ACTH produces a very slight depressive effect on the skin reactions, but this is so slight that it is of no practical significance. (4) To treat exceptionally severe cases which have not responded to the usual methods of treatment. This indication is quite rare in childhood.

In eczema the method of choice is oral administration of cortisone, and the dosage for this is the same as in asthma. On occasion it may be necessary, for example in a vomiting child, to use intramuscular cortisone or intramuscular ACTH, the dosage again being the same as for asthma. Again it should be emphasized that the recommended dosages apply only to the first few days of treatment; as the patient responds, the dosage should be rapidly decreased to a maintenance dosage which is frequently no more than 25 mgm. of cortisone a day. As has been pointed out by Hill,[8] the treatment should not be continued if it is found that over 75 mgm. a day is required. Hill feels that with 75 mgm. or

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less a day the chances of undesirable side-effects are small, but above this dosage the risks are too great to justify continuing the drug.

Series of cases have been reported by Hill,[8] Glaser,[9] Gelfand[10] and others. Downing[11] has reviewed the use of ACTH and cortisone in dermatology.

Cortisone ointment is useless in the treatment of eczema.[9] Hydrocortisone ointment, however, has been found to be extremely useful. Sulzberger *et al.*[12] reported 30 cases of atopic dermatitis treated with hydrocortisone ointment. Only six of these cases were in children. The response with the use of this drug was quite dramatic. Witten *et al.*[13] have reported 30 cases treated with 2½% ointment, and McCorriston[14] has reported 104 infants treated with either 1 or 2½% hydrocortisone ointment with dramatic results. Again it should be emphasized that both oral cortisone and hydrocortisone ointment give only temporary benefit while they are actually in use and that it is never justifiable to use these ointments without using the accepted anti-allergic methods of treatment in order to attempt a permanent good result.

Urticaria.—It is almost never necessary to use ACTH or cortisone in urticaria. However, the use of these drugs would be justified in a very severe acute attack of urticaria which was not responding to other methods of treatment. This is rarely necessary in children.

ACTH and cortisone may be used in other manifestations of allergy in childhood, for example, severe penicillin reactions, but these will not be discussed in this paper.

Discussion

Certain principles should be followed in using ACTH and cortisone in allergies in childhood. (1) These drugs should definitely not be used in those conditions where the standard methods of symptomatic relief such as administration of adrenaline, aminophylline and ephedrine are effective. The danger of undesirable side-effects is too great and the drugs are too expensive to warrant their use when safer and cheaper means are available. (2) These drugs do not in any way replace the accepted methods of anti-allergic therapy such as dietary control, environmental correction and hyposensitization procedures. One is no more justified in treating a case of allergy with ACTH and cortisone without applying the other measures of investigation and treatment which have been proved to produce good results than one is justified in treating a case of acute rheumatic fever with aspirin alone, ignoring all the other measures of investigation and treatment for this condition. (3) The parents of the patient should be warned that these drugs give temporary and symptomatic relief only. Otherwise the other methods of treatment are apt to be ignored by the parents in their enthusiasm at seeing the dramatic results which often follow the use of these drugs. When the drugs are later discontinued the condition is very likely to revert to its former status. (4) The lowest dosage possible to obtain a reasonable amount of relief should always be used. Larger doses are apt to cause undesirable side-effects, whereas relatively small doses often give sufficient relief to make the patient comfortable. (5) These drugs should never be stopped quickly; this is particularly important when they have been used in large dosage. The dose should be gradually decreased over a period of a few days to allow the adrenal cortex to revert to its normal state. (6) If the patient is receiving cortisone and requires an anæsthetic, the dosage of cortisone should be increased by at least 50%, preferably for a day or two before the anæsthesia, on the day of anæsthesia and for several days afterwards.[8, 15] The same precautions must be taken if a patient has been receiving cortisone within a few months prior to anæsthesia. Deaths have been reported as a result of ignoring this warning.

Summary and Conclusions

The use of ACTH and cortisone in the major allergies of childhood, namely asthma, hay fever, eczema and urticaria, has been reviewed. The indications for the use of these drugs and certain principles of treatment have been listed. It is concluded that, while these two drugs are very useful in the treatment of childhood allergies, they have very definite limitations; in no case should they be used as replacement for the accepted methods of anti-allergic therapy.

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CANADIAN INTERNATIONAL TRADE FAIR

The 1955 Canadian International Trade Fair, to be held in Toronto from May 30 to June 10, will contain exhibits of laboratory equipment, x-ray equipment, dental and surgical instruments, hearing aids and teaching aids such as foam rubber anatomical models. There will be exhibits of scientific material not only from Canada but also from the United Kingdom, United States, Germany and Czechoslovakia.

Canad. M. A. J.
May 15, 1955, vol. 72

THE CONCENTRATION OF CHLORAMPHENICOL IN HUMAN TISSUE*

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" . . . . THE PHYSICIAN must insure that the antibiotic reaches the organisms in the body in a concentration high enough to destroy them. This problem is often neglected." (Fleming.[1])

In a series of papers[2 to 5] designed to investigate the potentialities of chloramphenicol, it became clear that the cornerstone to an understanding of its action and usefulness in the treatment of disease lay in the statement quoted above. The present investigation deals with the crux of the matter, for an attempt has been made to find what levels this antibiotic will attain in human tissue after reasonable—and unreasonable—dosages.

Post-mortem material was chosen, when the necessary time interval between last dose and the onset of death could be determined. By doing so, it was hoped that the survey would enable an evaluation of the possible variation in concentration in different tissues to be made. Only cases in which contamination by other antibiotics had not taken place were selected—unfortunately, extremely difficult to acquire.

It is possible that the failing circulation in a body preoccupied by dying might reflect on the antibiotic values actually ascertained. However, an awareness of this factor led to an examination of such cross-checks as could be found, and these appear to indicate that the approach was acceptable.

METHODS AND MATERIALS

The tissues selected at post mortem were washed in running tap water, then dried in a towel. Special care was taken to make sure that gut contents were cleared away from that section of the ileum chosen for the experiments. Ten grams of each tissue were carefully weighed out. The tissues were next minced, and emptied into porcelain evaporating dishes, then dried on a sand bath at 50° C. The dry contents were ground to powder in a mortar, and transferred to sterile 7" x 1" test tubes. Fifteen ml. of peptone water (Difco) were added and the contents kept in a boiling water bath for 30 minutes. On removal, the meniscus was brought up to the mark by additional peptone water if required, and the tubes were allowed to stand until the sediment settled. The supernatant was pipetted off with a sterile Pasteur pipette, care being taken to avoid the fatty layer, and transferred to sterile conical centrifuge tubes, which after capping were spun for 15 minutes. Again, the supernatant was pipetted into sterile test tubes which were then placed in a boiling water-bath for 20 minutes. On removal, the tubes were incubated overnight at 37° C. for sterility. It should be remembered that chloramphenicol will withstand boiling for an hour without degradation.

The antibiotic content of the supernatant was estimated as follows: Ten sterile 3 x 18 mm. test tubes were set out in a rack and, using sterile 1 ml. calibrated pipettes, the following quantities of supernatant were added to the respective test tubes.

1st	1.0 ml.	6th	0.1 ml.
2nd	0.8 ml.	7th	0.05 ml.
3rd	0.6 ml.	8th	0.05 ml.
4th	0.4 ml.	9th	0.2 ml. of a 1/10 dilution.
5th	0.2 ml.	10th	0.2 ml. of a 1/10 dilution.

Tubes 1-6 were brought up to a total volume of 1 ml. by the addition of peptone water; tube 7 had 0.7 ml. of peptone water added; tube 8, 0.95 ml.; tube 9, 0.6 ml.; and tube 10, 0.8 ml. This gives a series of dilutions of: 10/10, 8/10, 6/10, 4/10, 2/10, 1/10, 1/14, 1/20, 1/30, 1/40.

To each of the test tubes was now added 1 loopful of an overnight peptone water culture of El Tor vibrio. This organism is sensitive to chloramphenicol at a concentration of 0.5 microgram per ml. At this sensitivity, the dilutions give range of antibiotic concentration of: 0.5, 0.6, 0.8, 1.25, 2.5, 5, 7, 10, 15 and 20 micrograms per ml.

The cultures were incubated overnight at 37° C., and the end-point was taken as the first tube showing no growth. Tissue concentration was corrected for the dilution factor.

Normal human tissue treated in the above manner does not appear to contain inhibitory substances against the El Tor vibrio. In two control cases, growth was obtained in a 1/1 dilution in all examined specimens.

Provided care is taken to avoid fat in transferring the supernatants, a slight cloudiness of the treated medium does not interfere with the estimation of the end point. The vibrio used forms a characteristic surface pellicle in tissue extracted peptone water, which makes the presence or absence of growth easy to determine.

RESULTS

Case 1 (Table I) demonstrates the rapid rise of the antibiotic level in lung, spleen, and gut, all organs with a complex vascular bed; a moderate quantity in heart muscle; and little in the liver and kidneys. By the third hour (Case 2) the picture has changed. The concentrations in lung and spleen are falling; the level in the gut is still high, that in kidney, liver, and heart muscle markedly increased, and the concentration in the brain tissue highest of all. At 5 hours (Case 3) the lung and spleen content are the same as at the third hour; the concentration in the gut has levelled to a figure equivalent to that in the lung; the amount found in the liver approximates the third-hour figure; the content in the heart has risen appreciably; the concentration in the brain is still very high, and the amount in the kidneys has risen markedly.

By the twelfth hour (Case 4), only liver, kidney and gut contain an amount of antibiotic that would be inhibitory to most of the salmonellæ, shigellæ, coliforms and probably some of the pathogenic streptococci.

Case 5 demonstrates the lack of effective tissue concentration following a "one gram a day" regimen, affording further condemnation of this practice with chloramphenicol.

*From the Department of Pathology, Halifax Infirmary, Halifax, Nova Scotia.

TABLE I.

CONCENTRATION OF CHLORAMPHENICOL FOUND IN HUMAN TISSUE AFTER VARIOUS DOSES, AND AT VARYING TIMES AFTER THE DOSAGE

Case No.	Dose of chloramphenicol in mgm. per kilo per day	Individual dose intervals in hours	Time in hrs. of last dose before death	Antibiotic tissue concentration in micrograms per gm. of wet tissue						
				Lung	Heart muscle	Liver	Spleen	Kidney	Brain	Gut
1	100	6	1	12	5	2.5	13.0	1.5	2	12
2	150	8	3	7	11	10.0	7.0	6.0	20	18
3	200	3	5	7	20	8.0	7.0	33.0	30	8
4	100	6	12	0	1	4.0	0.0	4.0	—	4
5	15	6	6	0	0	1.25	0.5	1.0	—	0

DISCUSSION

There are three dominant factors for evaluation when antibiotic therapy is considered: the resistance of the organism, the patency of the vascular tree supplying the tissue under treatment, and the concentration of antibacterial substance achieved per unit of tissue. On the first two, there is reasonable knowledge, but on the last, except for experimental animal work, little relevant to the human. This restriction on our information has arisen from the chemical instability of the antibiotics with the exception of chloramphenicol, which is amenable to the demands of this type of inquiry.

It would appear that the concentration of chloramphenicol varies between types of tissue, and that this variable is further influenced by time. The lung, spleen and gut, highly vascular organs, show changes that mimic published serum level curves.[6] This is not so with the second set of tissues: heart muscle, liver, kidney and brain, all with a less florid vascular tree. Maximal concentrations in these are achieved from three to five hours after a dose, and retention of the antibiotic in moderate amounts continues for at least 12 hours.

The high concentration found in the brain substance is a confirmation of the clinical impression that in meningitis it may be the drug of choice.[7] Further confirmation of parallel observations may be seen in the behaviour of the kidney to this drug. It will be noted that the time of maximum renal tissue concentration is five hours. This coincides with the period of maximum urinary output.[6] It is doubtful whether this "peaking" of renal tissue values and urine concentration is due to accumulation within that organ, followed by relatively sudden release, or rather to an increasing tempo of release by the highly vascularized organs reaching an apex about the fifth hour, the kidney reflecting this flux.

A consideration of the variations in chloramphenicol tissue values offers an explanation of the disappointments met with when dosage appears adequate and resistance of the organism within acceptable limits. An infection of the lung with a *Staphylococcus aureus*, having a resistance of 10 micrograms, treated with a dose of chloramphenicol at 100 mgm. per kilo per day in divided doses, would produce a concentration of antibiotic only 2 micrograms higher than the resistance, a level which is apparently not maintained for much more than an hour—obviously an inadequate regimen. On the other hand, a pneumonia due to a coliform bacillus whose resistance is 3 micrograms would be well covered by the same dose for as long as five hours. It takes little imagination to evoke reasonable clarification of other apparent therapeutic anomalies.

In the opening paragraph of this discussion, three factors were given which appeared to control the rational use of an antibiotic. The observations contained in this paper suggest the absolute necessity of their appreciation if the best results are to be obtained from the use of chloramphenicol in the treatment of infections. To say more would belabour the point.

SUMMARY

1. A method of estimating the content of chloramphenicol in human tissue is described.

2. The values found for certain tissues with varying doses are given. The relationship of these findings to time is discussed.

3. The necessity for the appreciation of chloramphenicol tissue concentration in regard to therapeutic success is outlined.

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SWEDISH HEALTH SERVICE

The National Health Insurance Scheme, introduced in Sweden on January 1, 1955, has not brought about any considerable increase in the number of cases of sickness reported, as had been expected in many quarters.—*SIP Bulletin*, March 5, 1955.

Canad. M. A. J.
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(Information regarding contributions and advertising will be found on the second page following the reading material.)

Editorials

DIAMOX (ACETAZOLEAMIDE)

The need for an effective oral diuretic agent in the treatment of congestive heart failure has stimulated continuing research. Diamox* (2-acetylamino-1, 3, 4-thiadiazole-5-sulfonamide), a heterocyclic sulfonamide compound, is capable of increasing the urinary excretion of sodium ion and has been used as a diuretic in heart failure.

The pharmacological action of Diamox is attributable to its free sulfonamide group which inhibits the action of the enzyme carbonic anhydrase.[1] This enzyme is most generally known for its position in respiratory physiology as the catalyst of the reversible reaction $H_2CO_3 \rightleftarrows H_2O + CO_2$ which facilitates transfer of carbon dioxide from tissues to venous blood to pulmonary alveoli. Carbonic anhydrase is also present in the cells of the renal tubules, where it allows the excretion of acid in the urine.[2] Maintenance of a normal acid-base balance in the body fluids requires the elimination of hydrogen ion by the kidney. The tubular cells derive hydrogen ion from carbonic acid, excrete it into the tubular lumen and accept sodium ion from the glomerular filtrate to replace the hydrogen ion. In this way acid is excreted and base, as sodium, is retained. When the action of carbonic anhydrase is inhibited by Diamox, carbonic acid is no longer available to the tubular cells as a source of hydrogen ion. There results a decreased urinary excretion of hydrogen ion and an increased excretion of sodium ion. The urine becomes more alkaline and the blood more acid. As in mercurial diuresis, the excretion of sodium is accompanied by the excretion of water. The dose of Diamox which produces these renal effects does not interfere with the pulmonary elimination of carbon dioxide.

Schwartz[3] used sulfanilamide as a carbonic anhydrase inhibitor and observed diuresis in three patients with congestive heart failure. He considered this drug too toxic for general use as a diuretic. Synthesis of heterocyclic sulfonamide compounds increased the potency and reduced the toxicity. The newer product, Diamox, was tried in congestive heart failure by Friedberg *et al.*[4] with promising results. There was an increase in urine volume, decrease in acidity, and increase in sodium excretion. The drug was given orally in a dosage of 250 milligrams daily or in interrupted courses of 250 milligrams three times daily for three days without diminution in effect or serious side-reactions.

Detailed balance studies by Leaf *et al.*[5] indicated that refractoriness to the drug did develop and was associated with systemic acidosis brought about by the excessive renal elimination of base. Although inhibition of urinary acidification was always effected, renal excretion of sodium was not always increased. The diuretic effect was small compared with that from a single dose of parenteral mercurial diuretic. Clinical studies by Relman *et al.*[6] failed to confirm the therapeutic effectiveness of Diamox in patients admitted to hospital in congestive heart failure. Only one patient out of twenty-six had a large enough diuresis to become free of cardiac œdema.

Failure of this drug to perform as good a job as mercurial diuretics in the treatment of advanced heart failure does not imply that it may not be useful in the management of milder cases treated in the office or out-patient clinic. Experience in this sphere is not extensive enough to allow a firm decision. It is possible that a minority of patients will have some real benefit. It is probable that in heart failure due to chronic pulmonary disease, the excess CO_2 content of the blood will prevent the development of refractoriness and allow continuing diuresis.

*Proprietary name, Lederle Laboratories, for acetazoleamide.

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ACUTE RHEUMATISM

An outstanding report on the treatment of acute rheumatism in children has appeared simultaneously in the *British Medical Journal* issue of March 5 and the March issue of *Circulation*. This is a report of the first stage in a remarkable co-operative clinical trial designed and carried out by two groups of investigators simultaneously in the United Kingdom and in America. The U.K. study was sponsored by the Rheumatic Fever Working Party of the Medical Research Council and the American study by a subcommittee of the American Heart Association. Canada participated in the American study through a Toronto group (Dr. John D. Keith and his associates) and a grant from the Canadian Arthritis and Rheumatism Society. The questions which the trial, which involved 242 children under 16 in the U.K. and 263 in the U.S.A. and Canada, is designed to answer are: (1) What is the relative effectiveness of cortisone and adrenocorticotropin (ACTH) and of aspirin in altering the course of acute rheumatic fever or in suppressing its clinical manifestations? (2) What is the relative effectiveness of the three agents in preventing rheumatic heart disease? The present report is concerned only with question (1), and compares the effects of the drugs on the acute course of rheumatic fever through 13 weeks from the start of treatment, and on the persistence and development of rheumatic heart disease through one year.

To appreciate the great care taken in planning the study so as to ensure comparability of results, and the high quality of reporting achieved, the original report must be read. Only a brief summary of the main conclusions can be given here. There was no evidence that any of the three agents resulted in uniform termination of the disease; on all schedules, some patients developed fresh manifestations during treatment. ACTH and cortisone caused a more rapid fall in erythrocyte sedimentation rate and quicker disappearance of nodules and of soft apical systolic murmurs, but this was counterbalanced by a greater tendency to later rise in E.S.R. or reappearance of nodules. Other factors, such as temperature, pulse rate during sleep, or joint changes, were equally affected by all three agents. After one year, there was no significant difference between the three treatment groups as regards the status of the heart. There were only six deaths among all groups.

It would seem from this report that ACTH and cortisone have added practically nothing except a higher proportion of side-effects (moonface, hirsutism, acne or striæ developed in the great majority of hormone-treated cases) to the treatment of this disturbingly common condition, since it is unlikely that continued follow-up of the cases will tip the balance far in favour of the hormones. There is, of course, always the possibility that the continued development of new synthetic analogues of cortisone and other steroids may eventually make available a hormone with more powerful antirheumatic or anti-inflammatory properties. Ward and his colleagues (*Proc. Staff Meet., Mayo Clin.*, 29: 649, 1955) suggest this possibility for rheumatoid arthritis in reporting the enhanced antirheumatic effect of 9-alpha-fluorohydrocortisone acetate, unfortunately counterbalanced by the more disturbing action of this compound on electrolyte balance.

In the meanwhile, emphasis must still rest on prevention of acute rheumatism and its recurrences through control of streptococcal infections (as recently outlined by the American Heart Association in the February issue of *Circulation*). It remains to express the wish that the splendid co-operation shown in this report may develop, to the greater credit of Anglo-Saxon medicine as a whole.

RESEARCH IN PSYCHOPHARMACOLOGY

When one scientific discipline impinges upon another, there is usually an energizing of both. Unfortunately this cannot be enacted by fiat, but depends upon many factors such as the concurrence of technical advances and perceived needs. In the fundamental sciences this process usually goes unheralded and is recognized only by the specialists concerned. When a basic science contributes to revolutionary changes in the practice of medicine or the concept of disease, it is stop press news and everyone's concern.

Such a movement has been taking place in pharmacology and psychiatry with increasing speed in the past 12 months. Therefore the research conference organized by the Department of Psychiatry of McGill University and held on March 26 in Montreal served a topical purpose. It was the first conference held in Canada under

Canad. M. A. J.
May 15, 1955, vol. 72

the rubric of psychopharmacology. That may be enough to commend or condemn it in the eyes of semantic radicals or conservatives, but a better neologism remains to be coined to epitomize the developments taking place. In any event, the enthusiastic reception given the papers left no doubt as to the community of interest of psychiatrists, pharmacologists, physiologists and biochemists in the investigation of new drugs.

In his opening remarks the chairman drew attention to certain undesirable phenomena which attended the introduction of ACTH and cortisone as therapeutic agents. The atmosphere then was almost revivalist, so high were hopes raised by the initial reporting and reception of the dramatic results. The fact was that a great advance in knowledge had been made, though the new products were not the fabulous cure for many diseases as at first thought. With this recent experience in mind, the current advances in the application of drugs to psychiatry should be viewed soberly.

An erudite and historical review of the subject, which hereafter will be unashamedly labelled psychopharmacology, was first presented. This was followed by papers devoted to the experimental therapeutic aspect of new drugs. Authoritative accounts of the results obtained with chlorpromazine (Largactil) were first presented. The influence of this agent in terminating acute psychotic attacks, in controlling agitation in patients, and in eliminating the need for restraint and emergency electroshock therapy was emphasized. Far from reducing the need for psychotherapy, this advance underlines the necessity for trained personnel at all levels because more patients become available and accessible to a psychological approach. There are therefore opportunities for study of patients at a stage of their illness not heretofore possible. Implications for psychiatric theory are already emerging and one may anticipate new facts upon which old theories may be tested and from which new formulations may arise.

What has just been said also applies to the results of use of rauwolfia derivatives in psychiatry. These products are employed in larger doses than in the treatment of hypertension and result at times in some uncomfortable but not serious toxic symptoms. Jaundice, which is an occasional complication with chlorpromazine, does not occur.

Observations on the production of psychotic symptoms by the drugs mescaline and d-lysergic acid diethylamide (L.S.D.) and other allied compounds were described. These chemicals, collectively subsumed under the term "hallucinogens," do not reproduce the exact picture of any classifiable mental disease. However, they elicit changes of a sufficiently bizarre and psychotic-like nature; the transient nature of the changes warrants their use as tools for investigation. Whether the body produces substances of a similar structure in mentally disturbed people remains to be proven. Meanwhile rewarding insight is being gained into the disturbed reactions of mentally sound people under controlled conditions. These drugs and those referred to earlier are providing fresh tools for exploring psychiatric problems and are supplying an impetus to an experimental approach in a field notoriously resistant to experiment. Already much has been learned about the locus and manner of action of these drugs by refined metabolic and neurophysiological techniques, as the closing papers of the conference indicated.

An era of great promise has thus opened in psychiatry, but it must not be expected to compare with the chemotherapeutic developments in medicine. It is still more complicated and at the same time less comprehensive. It will require the integration of many other approaches, psychological, psychodynamic and social, before the task of comprehending and helping errant man is fairly achieved.

R.A.C.

Editorial Comments

FOOTWEAR AND COMFORT

If, like the natives of tropical and subtropical climates, we could go unshod, painful and disabling feet would seldom be encountered. As that is not possible in city conditions, or in the winter-time of Canada, the use of some form of footwear must be accepted as inevitable. In this matter, there is a conflict between the requirements of comfort and those of style. To the feminine half of the population a smart appearance is *de rigueur*, and in adolescence at least the male section is almost equally susceptible. The child, being relatively unselfconscious, as well as more adaptable, wears comfortable shoes and does not suffer. It will be unanimously admitted that there is much room for improvement in the design of footwear, especially that of women.

An interesting article by Haines and McDougall (*Lancet*, 2: 1308, 1954) makes an attempt to analyze the principles involved in adequate shoeing, and—probably for the first time—applies experimental technique. The authors assume that the essentials of a shoe are "a sole that makes contact with the ground, and a system of attachments that hold the sole to the foot." They made an experimental sandal consisting of a thin layer of leather over a thick layer of crêpe rubber. By a series of straps of variable width and attachments, the essentials of many types of footwear could be reproduced.

Slipping of the foot backwards could be controlled by an ankle strap passing beneath the malleoli and above the projection of the heel. Forward slipping was most effectively controlled by a strap passing over the dorsal aspect of the tarsal wedge, the natural wedge. If this tarsal strap is not present, as in the court shoe or pump, forward displacement of the foot can be prevented only by using the toes as a wedge which is forced into the forepart of the shoe. A strap in this position must be kept tight and must be narrower anteriorly than posteriorly. A "tensionmeter" was devised to measure the pressure exerted by this digital strap on the toes. It was found that this tension amounted to about three pounds when the subject was walking on the level, whereas in trying to walk downhill in high heels the tension of the strap and thus the pressure on the toes rose to six or seven pounds.

Ideally, there should be no pressure on the toes. This calls for either an open-toed sandal or a very large built-up toe section. The "straight inner edge," while undoubtedly relieving pressure on the first metatarso-phalangeal joint, tends to throw undue pressure on the lateral toes, and this may cause, especially with an incurving little toe, discomfort as great as that produced by hallux valgus.

The problem of footwear is a very difficult one. Feet are as individual as faces, and the left and right feet may differ from one another as much as or more than the right and left halves of the face. Theoretically, footwear should be "custom-made," but this is not economically feasible. A certain amount of standardization will always be required. That makes it all the more necessary that further investigation of the foot should be carried out, from the physiological or functional point of view rather than from the anatomical or structural. As far as we know, there has been no systematic study of age changes in the foot. With diminishing circulation there come thinning of the skin and atrophy of the fibro-fatty cushions that act as shock absorbers. These changes are readily noted in the hands, but are usually ignored in the feet, although as weight-bearing organs the feet have a far more arduous task to perform. The misconception that the foot is provided with arches is as prevalent as ever; the foot is a very beautiful arrangement of springs which tend to lose their resiliency as age advances; it has a complex system of joints, and joints must be used if they are to retain their health. A shoe should be a garment, not a splint.

TETANUS TOXOID

It will be recalled that last September (*Canad. M. A. J.*, 71: 287, 1954) we drew attention to a Baltimore study of the duration of immunity to tetanus conferred by wartime inoculation. In the April issue of the *Canadian Journal of Public Health*, a similar study is described by Moss, Waters and Brown of the Connaught Medical Research Laboratories, with results closely resembling those obtained across the border.

The questions to which the Canadian authors sought an answer were: For how long is reasonable immunity conferred by the usual course of inoculation? (This, of course, is a fundamental question in the use of poliomyelitis vaccine and BCG as well.) Can an immunity waning after a number of years be satisfactorily enhanced by a booster dose of tetanus toxoid? Can it be enhanced rapidly enough to make the use of a booster dose acceptable as tetanus prophylaxis in case of injury?

The authors studied 100 ex-servicemen who had had no injection for tetanus since their discharge from the forces, usually 8 to 9 years previously. They took a sample of venous blood for titration, and found that only 3 persons (all of whom had a doubtful inoculation history) had less than 0.01 unit tetanus antitoxin per ml. in the blood. Altogether 40 had 0.1 unit or less, and therefore were presumably in an unsafe state of immunity. All the volunteers were given 1 ml. of tetanus toxoid (10 Lf) subcutaneously, and the blood was titrated again 7 days later. The result was very satisfactory, for all were now shown to have over 0.1 unit per ml., and therefore to be properly protected. Since the incubation period of tetanus, though subject to wide variations, may be taken as 10 days on an average, it is clear that a booster dose given after an injury to one of these volunteers would have sufficed to protect him against tetanus.

It is suggested that all ex-servicemen in industry be given a booster dose of tetanus toxoid now, and that the routine interval between a primary course and each booster dose be five years.

THE BAD-NEIGHBOUR POLICY

Giant atomic-powered fans along the northern border have been proposed to turn back bad weather from Canada. That is one of many ideas the Federal Advisory Committee on Weather Control has received.—*New York Times*, April 10, 1955.

Canad. M. A. J.
May 15, 1955, vol. 72

MEDICO-LEGAL

VARICOSE VEINS

T. L. FISHER, M.D.,* *Ottawa*

WHEN IS MINOR SURGERY MAJOR? The surgical treatment of varicose veins, whether by injection —uncommon now—or ligation or stripping, often is considered minor surgery.

In December 1952, a doctor, using spinal anæsthesia, ligated the lower superficial veins of a patient's right leg. He wanted to tie off the superficial epigastric vein which, however, he had difficulty identifying. While attempting to find it, "the junction of the saphenous and femoral vein was punctured" and a hæmorrhage began which, with the means at hand in the outpatient department, was controlled with difficulty. It was estimated that 1,000 c.c. of blood was lost. An attempt to ligate the bleeding point was accompanied by a recurrence of bleeding. Finally the bleeders were tied off. As soon as that was done, the patient cried out in severe pain and a nurse reported that the whole leg as far as she could see it was white. By evening the leg was cold and the patient was sent to a larger hospital where, the following afternoon, it was decided to explore the wound. Two ligatures were found around the femoral artery. Two weeks later a line of demarcation formed about six inches below the knee, and the leg had to be amputated below the knee.

In November 1953, a lawyer, acting for the patient, notified the first doctor that action would be taken against him. A writ was issued before the end of 1953. The facts of the case were considered by the Council of the Canadian Medical Protective Association; they were submitted, in addition, to two outstanding surgeons and it was the consensus that there was no reasonable possibility of a successful defence. Therefore, after considerable negotiation, settlement for $10,000 was made.

A second case.—In April 1953, a 33-year-old woman, the mother of four children, consulted a doctor because of swelling of both legs. He decided that the cause was varicosities and advised surgical treatment of the veins in both legs. Accordingly, in May 1953 the patient was taken to hospital to have a stripping operation done. The doctor reported that he arranged for a confrère to assist him because "he had done more of these than I had." An incision was made in the right groin

"to explore the saphenous vein. The incision did not expose this vein but was slightly lateral, with the result that we picked up a vessel which seemed to go directly into femoral vein. This was picked up, ligated and vein stripper inserted. The stripper did not come out where we expected at ankle and we presumed it had gone through wall of vein so we pulled it through with intention of getting remainder of vein from below. The long saphenous vein was opened at the ankle and vein stripper inserted which came out at upper end of this vein in inguinal region in fat of medial edge of our inguinal incision. This vein was then stripped from below and removed."

As soon as the patient recovered from the anæsthesia she complained of severe cramp in the right leg and loss of circulation and coldness of right foot and lower leg. She was sent to a larger hospital and, ten days later, the leg was amputated below the knee.

In August of that year, through a lawyer, the patient made a claim for $15,000 for the loss of the leg. It was the opinion of counsel that "This is unquestionably a case for settlement, if it can be negotiated, for there is no real defence on liability." After considerable negotiation, settlement was effected for a total of $9,750 and a release was obtained. The total cost of the claim, settlement and legal costs was $10,540.

Elective surgery, no matter how minor, should never be undertaken without realization of possible complications and ability to deal with them.

When is minor surgery major?

*Secretary-Treasurer, Canadian Medical Protective Association.

Association Notes

NOTICE

AMENDMENTS TO THE BY-LAWS

In accordance with Chapter XVII, Section 2 of the By-Laws of the Canadian Medical Association, the Committee on By-Laws recommends the following amendments to the By-laws for ratification at the 88th Annual Meeting:

CHAPTER VI. (Membership and Discipline)

Section (2) (a) amend by adding the following paragraph:

"Where his fee remains unpaid on the first day of July of the current year, his name shall be removed from the list of members of the Association and his membership shall stand suspended without further action, but unless his membership has been suspended or cancelled on other grounds, his name shall be restored to the list of members and his suspension shall stand lifted on payment of his fees which are in arrears for the current year"

(2) (b) amend by deleting the words:

"disgraceful conduct" and substituting "conduct which the General Council considers unethical"

(2) (c) amend by deleting the words:

"disgraceful conduct" and substituting "conduct which the General Council considers unethical"

CHAPTER XI. (Officers, Officials and Executive Committee)

Section (3) (Duties and powers of the Nominating Committee)

Subsection (2) amend by deleting the words of this subsection and substituting:

"Nomination of an Executive Committee which, in addition to those who are members ex officio (see Chapter XIII, Section 6), shall consist of thirteen members drawn from the General Council and geographically distributed as follows: three shall be resident in the Province of Ontario, two shall be resident in the Province of Quebec, and one shall be resident in each of the eight other Provinces"

CHAPTER XII. (Duties of Elective Officers and Appointive Officials)

Section (1) (Duties of the President) amend by deleting the words:

"its Executive or its General Council" at lines 4 and 5.

Section (4) (Duties of the Chairman of the General Council) amend by adding the words at the end of the first sentence:

"and shall represent the General Council as and when required" to make the sentence now read, "The Chairman of the General Council shall preside at all meetings of the General Council and shall represent the General Council as and when required."

MEDICAL SOCIETIES

CANADIAN HEART ASSOCIATION, INC. – SOCIETE CANADIENNE DE CARDIOLOGIE

The following is the programme for the eighth annual meeting of the Canadian Heart Association, Inc., to be held in the Hospital for Sick Children, Toronto, on June 24 and 25, 1955.

Friday, June 24

9.30 a.m. – Annual business meeting.

2.00 p.m. – Afternoon Session—Joint Meeting with the Canadian Rheumatism Association.

2.00 p.m. – Cardiac Involvement in Rheumatoid Arthritis and Ankylosing Spondylitis. Hugh A. Smythe, Toronto.

2.30 p.m. – Observations on the Use of Metacortandracin in Rheumatic Disease. Phillip S. Rosen, Toronto.

3.00 p.m. – Metacortandracin in Rheumatic Diseases. R. Dussault, J. Blais, R. Demers, J. Durivage, L. Long, and de G. Vaillancourt, Montreal.

3.30 p.m. – Serious Toxic Manifestations of Prolonged Hydrazaline (Apresoline) Therapy. J. D. Morrow, Toronto.

4.00 p.m. – Selection of Patients for Mitral Commissurotomy. Paul Wood, National Heart Hospital, London, England.

Saturday, June 25

Morning Session

9.30 a.m. – Panel Discussion: Is Ordinary Effort a Precipitating Factor in Coronary Occlusion? Introduction. George F. Strong, Vancouver. Clinical Aspects. William Evans, London, Eng.; Harold N. Segall, Montreal. Pathological Aspects. J. C. Paterson, London; H. J. Barrie, Toronto.

11.30 a.m. – Anticoagulants in Coronary Disease. A. R. Gilchrist, Edinburgh.

Afternoon Session

2.00 p.m. – Artificial Heart-Lung Pump in Congenital Heart Surgery. W. T. Mustard, Toronto.

2.30 p.m. – Hypothermia in Heart Surgery. W. G. Bigelow, Toronto.

3.00 p.m. – Selective Angiocardiography in Infants and Children. Richard D. Rowe, Toronto.

3.30 p.m. – Atrial Septal Defects with Special Reference to Atrioventricularis Communis. John D. Keith, Toronto.

CANADIAN RHEUMATISM ASSOCIATION

The programme for the 1955 annual meeting of the Canadian Rheumatism Association, which will be held in Toronto on June 24 and 25, is as follows. The scientific sessions will be open meetings, not confined to Association members.

Friday Morning, June 24

Private Dining Room No. 10
Royal York Hotel

9.00 a.m. – Ultra-sound Wave Therapy in Soft Tissue Rheumatism. Dr. Walter Ruhman, Montreal.

9.30 a.m. – Spontaneous Rupture of the Extensor Pollicis Longus Tendon in Rheumatoid Arthritis. Drs. W. R. Harris and Glen A. MacDónald, Toronto.

10.00 a.m. – Sjögren's Syndrome—An Ocular Complication of Rheumatoid Arthritis. Dr. A. J. Elliot, Professor of Ophthalmology, University of Toronto.

10.30 a.m. – Operative Procedures of Value in Rheumatoid Arthritis (Review of Toronto General Hospital Cases). Dr. W. R. Harris, Toronto.

11.00 a.m. – A Report on the U.K. Controlled Study on Comparative Effects of Cortisone and Aspirin in Rheumatoid Arthritis. Dr. Malcolm Thompson, Boston, Mass.

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11.30 a.m. – Meeting of Council of the Canadian Rheumatism Association. (Closed meeting —Council members only.)

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Friday Afternoon

Joint Meeting with the Canadian Heart Association
Lecture Theatre, Hospital for Sick Children

2.00 p.m. – Cardiac Involvement in Rheumatoid Arthritis and Ankylosing Spondylitis. Dr. Hugh A. Smythe, Toronto.

2.30 p.m. – Observations on the Use of Metacortandracin in Rheumatic Disease. Dr. Phillip S. Rosen, Toronto.

3.00 p.m. – Metacortandracin in Rheumatic Diseases. Doctors R. Dussault, J. Blais, R. Demers, J. Durivage, L. Long, and de G. Vaillancourt, Montreal.

3.30 p.m. – Serious Toxic Manifestations of Prolonged Hydralazine (Apresoline) Therapy. Dr. J. D. Morrow, Toronto.

4.00 p.m. – Selection of Patients for Mitral Commissurotomy. Dr. Paul Wood, London, England.

Saturday Morning, June 25

Private Dining Room No. 10
Royal York Hotel

9.00 a.m. — A Clinical Review of Rheumatic Diseases, Diagnosis and Treatment. Dr. Douglas Taylor, Toronto.

9.30 a.m. — Assessment of Therapeutic Agents in Rheumatoid Arthritis. Dr. L. Mandel, Ottawa.

10.00 a.m. — Pigmented Villonodular Synovitis. Dr. J. N. Swanson, Toronto.

10.30 a.m. — The Sensitized Sheep Cell Reaction in Rheumatoid Arthritis. Dr. R. W. Lamont-Havers, Vancouver.

11.00 a.m. — Annual General Meeting of the Canadian Rheumatism Association (Association members only).

CORRESPONDENCE

COMPULSORY TREATMENT OF TUBERCULOSIS

To the Editor:

It was rather disturbing to read the article by Dr. J. E. Hiltz (December 1954), and to learn that in Nova Scotia, in this year of grace, the public are still obsessed with the Biblical-Pasteurian concept of the infectivity of disease, and have gone so far as to demand the compulsory isolation of persons suffering from tuberculosis.

Dr. Hiltz excuses this by drawing a parallel between this legislation and that requiring the restraint of homicidal lunatics, and the licensing of firearms and restaurants. A more exact parallel, which he might have mentioned, would be the compulsory isolation of cases of smallpox. There is certainly a theoretical risk that a person with open tuberculosis can infect a susceptible person, but there the comparison ends, because the risk to communal health in the case of tuberculosis is so very much smaller as to be negligible.

Mass x-ray surveys reveal that there are one to five cases of open tuberculosis among every 100 persons. In India, Indonesia and parts of Africa it is more like 10%; in Canada it is perhaps only 0.1%. But whatever the figure, it means that there are in fact dozens of open cases of tuberculosis mingling freely with the rest of the population. The disease is almost symptomless in old people and rarely is there any question of isolating them. What harm are we doing if we allow to remain with these others the one or two persons too psychologically maladjusted to submit to sanatorium treatment? What good will it do to hound poor wretches to prison where it is exceedingly unlikely they will improve, burning, as they must be, with righteous indignation? If a man does not want treatment that is his misfortune, but do not let us delude ourselves that, in so refusing, he is thereby a special *extra* menace to the rest of the population.

One cannot but get the impression, reading between the lines of Dr. Hiltz's article, that the real reason why these people are locked up in Nova Scotia is because they are "not intelligent and co-operative," because they are "unwilling to conduct themselves" in conformity with Nova Scotian public opinion, not because they are in fact, in the legal sense, more liable, to use Dr. Hiltz's words, to "commit mayhem" than the rest of the population.

To deprive a man of his personal liberty is so serious a matter that anyone concerned with it, as our legal colleagues well know, must be very, very sure that his grounds are based on facts, not feelings. Our duty to prevent sickness does not give us a licence to persecute all those who do not conform to our ideas of behaviour. Our duty is to educate and lead public opinion, not to pander to popular demands based on an outworn and inexpert appreciation of the true situation.

Logically the next step in Nova Scotia should be to lock up all carriers of salmonella bacilli, and all persons with streptococcal throats. Both of these can cause equally fatal or permanently disabling diseases. The only reason, as far as I know, why such legislation is not likely to be introduced, is the fact that the public have no fear or loathing of these conditions in the way tuberculosis is feared and loathed. The difference is purely subjective, and is not based on any scientific reasoning. Yet in one case the person goes free, in the other he is the victim of man's hysteria.

The attempt to deal with the tuberculosis problem by the process of enforced isolation has long been abandoned in most countries. Is Nova Scotia right and the rest of the world wrong?

W. NORMAN TAYLOR, M.D.(Lond.), D.P.H.
Fort Hare,
Alice, C.P., South Africa,
March 25, 1955.

WATER SOFTENERS AND LOW-SODIUM DIETS

To the Editor:

In a letter to this column, Dr. E. L. Brown *(Canad. M.A.J.*, 72: 544, 1955) points out the importance of considering the source of water used in low-sodium diets with particular reference to the use of water softeners.

In an excellent paper by Ferguson and Kay *(Canad. M.A.J.*, 69: 491, 1953) this specific topic is dealt with in some detail. In this same article the importance of the sodium content in untreated water and in various beverages is also made clear.

ROBERT JACKSON, M.D.
Montreal General Hospital,
Montreal, Que.,
April 17, 1955.

INDIAN TOURS

To the Editor:

To increase friendship between East and West, in 1950 and again in 1951 I took a party of medical men and women from Great Britain and Western Europe by air for a five-week tour of India.

This year I am hoping to repeat the tour in November at an approximate cost of £298 per person. This will include return air fare from London, and travelling and living expenses in India. The normal cost of such a trip would be at least £600 per person. As the size of the party must be restricted to a reasonable number, may I ask any medical practitioner who is interested to write to me at once. Any doctor who joins the party may be accompanied by his relatives.

Any doctor who wishes to travel independently in India may take advantage of this chartered 'plane by paying only £160 return fare.

R. U. HINGORANI, M.B., B.S.
128 Harley Street,
London, W. 1, England,
March 31, 1955.

ABSTRACTS *from current literature*

MEDICINE

Absence of Tonsils as a Factor in the Development of Bulbar Poliomyelitis.

ANDERSON, G. W. AND RONDEAU, J. L.: J. A. M. A., 155: 1123, 1954.

The proportion of patients with bulbar poliomyelitis has supposedly increased in recent years and is greater in the older age groups. Many investigators have advanced evidence that a bulbar paralysis is more likely to develop in those who have undergone tonsillectomy during the month before the onset of poliomyelitis. Bodian has advanced the hypothesis of viræmia resulting from gastrointestinal absorption, with subsequent localization of the virus in the central nervous system by escape through capillary areas of special permeability. According to this concept the usual bulbar form develops in persons whose capillaries of the medullary area are more permeable than those of the spinal cord.

In 1941 Top and Vaughan reported an increased incidence of bulbar poliomyelitis in the tonsillectomized. The present study is an attempt to confirm these authors' observations, and is based on epidemiological histories of 2,669 cases of poliomyelitis in a Minnesota epidemic in 1946. The cases of poliomyelitis were classified by type of involvement solely on the basis of history; evidence of difficulty in swallowing, breathing, phonation or other signs of involvement of the cranial nerves was taken to indicate bulbar poliomyelitis without attempting to distinguish between bulbar, bulbospinal or encephalitic forms. The cases of spinal disease were divided into severe and mild.

For all age groups, 71.4% of the 535 persons with bulbar involvement gave a history of tonsillectomy as compared with 28.2% of 936 severe spinal, 32.6% of 908 mild spinal and 34.8% of 290 non-paralytic cases. Even more significant is the fact that the difference holds at all ages and in both sexes and is actually greater in those under 15. The same basic data were analysed to show the distribution of the patients who had and who had not had tonsillectomy according to type of involvement; 36.6% of the former had bulbar involvement as contrasted with only 9.4% of the latter. From their figures the authors conclude that if recognizable poliomyelitis occurs in a child who still has his tonsils the chance is only 1 out of 12 that the infection will be bulbar, whereas if the child has had his tonsils out, the chance of bulbar involvement is more than 1 out of 3. The authors estimated the difference between the number of bulbar cases in the tonsillectomized patients and the number that might have been expected if this group had had the same proportion of bulbar involvement as had the non-tonsillectomized patients; there were 273 more bulbar cases in the entire group than might have been expected on this basis. Differences in frequency of bulbar infection in the two groups were not attributable to age, sex or economic differences.

Apart from the first month, the length of time after operation is not a factor in the high incidence of bulbar infections in poliomyelitis. Results also fail to support the idea of anæsthetic damage as a factor in the high bulbar rate. In discussing the concept that unrecognized central nervous system damage may have resulted from severing the tonsillar nerve fibres, the authors point out that if such a hypothesis was correct there would be more right leg involvement in patients who had had appendectomy, but the figures failed to support such an idea. The authors finally suggest that removal of the tonsils may have facilitated throat invasion through removal of some natural barrier and thus promoted a higher proportion of bulbar involvement.

The greater tendency for older patients to have a bulbar type of disease is due to the fact that they are more likely to have had their tonsils removed than are children; absence of tonsils rather than age conditions the bulbar type of response. The higher proportion of bulbar cases today compared with 30 years ago may well be associated with the shift in age distribution of poliomyelitis and the increased frequency of tonsil operations; lack of bulbar involvement in Egypt, Chile and Japan may be due to the almost invariable presence of tonsils at the ages at which the vast majority of the infections occur.

W. F. T. TATLOW

Clinical Evaluation of 6-Mercaptopurine in the Treatment of Leukæmia.

BURCHENAL, J. H. *et al.*: AM. J. M. SC., 228: 371, 1954.

The therapeutic activity of 6-mercaptopurine has been evaluated by the chemotherapy service at the Memorial Center for Cancer and Allied Diseases, in 269 patients with neoplastic disease. Of these, 140 had acute leukæmia; 8 had subacute, 18 chronic myelocytic, and 4 chronic lymphocytic leukæmia. The usual dose in children was 2.5 mgm. per kg. by mouth in a single daily dose; at this level very few toxic manifestations were observed. This dosage is usually also tolerated by adults, but in some patients there was evidence of bone marrow depression. At higher levels, severe depression of all formed elements of the marrow was occasionally a serious hazard, but in some patients, both children and adults, 5 to 7 mgm. per kg. was tolerated without difficulty. At 2.5 mgm. per kg. daily the antileukæmic effect of 6-mercaptopurine generally did not become manifest until 3 to 8 weeks of continuous treatment, although occasionally it acted more rapidly.

6-Mercaptopurine was of no practical value in chronic lymphocytic leukæmia, lymphosarcoma, Hodgkin's disease or metastatic carcinoma. In patients with metastatic reticulum cell sarcoma, slight temporary regression of tumour masses and subjective improvement were occasionally noted. In 11 of 12 patients in the early stages of chronic myelocytic leukæmia, 6-mercaptopurine was effective in producing satisfactory remissions with definite fall in white count, decrease in immature forms, rise in hæmoglobin value, and a decrease in splenomegaly and heptomegaly. Of 87 children with acute leukæmia, 41 had good clinical and hæmatological remissions and 16 had partial remissions; in 30 the treatment failed. The results in acute leukæmia in adults were not so satisfactory.

Apparently, 6-mercaptopurine adds another type of antileukæmic agent to the armamentarium of the clinician.

S. J. SHANE

Clinical Determination of Mitral Insufficiency when Associated with Mitral Stenosis.

JANTON, O. H. *et al.*: CIRCULATION, 10: 207, 1954.

Although pure mitral insufficiency and pure mitral stenosis appear to be two separate clinical entities, their apparently clear-cut dissimilarities are quickly lost when the two are combined. Mitral stenosis is the dynamic dominant and soon governs the clinical picture. However, certain dissimilarities remain to varying degrees in the individual patient and are useful in clinical evaluation. Preoperative detection of severer grades of mitral insufficiency associated with mitral stenosis is important, because the results of mitral valve operation are much poorer in patients with combined lesions than with pure mitral stenosis.

Two hundred operated cases of pure mitral stenosis and 47 operated cases of combined mitral stenosis and mitral insufficiency were studied. It was found that careful evaluation of the natural history, ausculatory

Canad. M. A. J.
May 15, 1955, vol. 72

findings, electrocardiogram and fluoroscopy permits a correct diagnosis of associated insufficiency in a majority of cases. However, 30% of 200 patients with pure mitral stenosis had a mitral systolic murmur as well as a diastolic murmur; it is in this group that the question of significant associated insufficiency arises. In such cases the intensity of the mitral systolic murmur is the most useful differential feature of auscultation. Systolic murmurs of grade 4 intensity and, less frequently, of grade 3 intensity, indicate significant associated mitral insufficiency. The natural history is also important, since systemic arterial embolization occurs less frequently with associated insufficiency than with pure stenosis. Furthermore, the major complaint in the case of mitral stenosis is dyspnœa, while with insufficiency it is fatigue.

The only value of the electrocardiogram in the differentiation of the predominance of mitral stenosis or mitral insufficiency is due to presence of left ventricular hypertrophy when insufficiency is predominant, and of right ventricular hypertrophy when stenosis is predominant. This examination is not always helpful, however, since about one-half of all patients with pure mitral stenosis in this study showed no electrocardiographic evidence of right ventricular preponderance.

It is evident, therefore, that there is no single clinical or laboratory procedure that will predict the predominance of mitral insufficiency over mitral stenosis. Rather, it is a matter of integrating the historical and laboratory features of each patient. S. J. SHANE

Chronic Barbiturate Intoxication.

FRAZER, H. F. *et al.*: A. M. A. ARCH. INT. MED., 94: 34, 1954.

This present work is an extension of the work of Isbell *et al.* on variations in the clinical picture of barbiturate addiction, withdrawal, and recovery. Five of the subjects figured in an earlier report, but 14 additional male volunteers, who were admitted to the U.S. Public Health Service Hospital in Lexington for addiction to opiates and chronic barbiturate intoxication, were also studied. The patients were continuously observed in a special closed ward throughout the study, and secobarbital was used by the oral route for the production of chronic intoxication.

The signs and symptoms of maintained barbiturate intoxication resembled those produced by alcoholic intoxication. Confusion, impairment of judgment, alternating mood swings, decreased ego control and marked regression in behaviour were found; the patients neglected their person, some had to be fed by attendants, and dysarthria, nystagmus, ataxia and diminished or absent reflexes were found on neurological examination. The authors found marked variation in the degree of intoxication and tolerance in different individuals. Withdrawal of barbiturates was abrupt and complete, and no treatment whatever was given except to two patients whose lives were considered to be in danger. The authors classified the withdrawal symptoms and signs as "major" convulsions and delirium, and "minor," and noted that only three out of the 19 patients escaped both convulsions and delirium. Between the eighth and thirtieth hour after the last dose of barbiturate "minor" symptoms started: these consisted of anxiety, involuntary twitching of muscles, coarse intention tremor, weakness, dizziness, distortions in visual perception, nausea and vomiting, insomnia, weight loss and precipitous falls in blood pressure. Convulsions developed in 79% of the patients, and during the convulsive phase 63% of the patients developed a psychosis which resembled alcoholic delirium tremens. Psychological tests performed during addiction revealed a severe impairment of coordination. Such persons would be very unsafe automobile drivers or operators of other potentially dangerous machines. During chronic barbiturate intoxication the electroencephalograms were abnormal in 98% of cases, with mixed rhythmic fast and slow activity. There was a dramatic and abrupt change in the electroencephalogram in the acute abstinence period; on the second day the background activity appeared to become more normal but it was interrupted by high-voltage paroxysmal discharges in over 40% of the records, this paroxysmal abnormality consisting of either high-voltage mixed spike and slow waves or of well-defined 4 c/s spike-and-dome complexes. The electroencephalograms had returned to normal in 72% of cases by the ninth day of abstinence. W. F. T. TATLOW

SURGERY

New Methods of Surgical Treatment of Degenerative Diseases of the Abdominal Aorta.

JULIAN, O. C. *et al.*: ANN. INT. MED., 41: 36, 1954.

Fourteen cases are presented in which the lower segment of the abdominal aorta bifurcation and a portion of the iliac vessels were resected and replaced by preserved homologous grafts. In 7 patients the operation was carried out for Leriche's syndrome (intermittent claudication of the lower extremities, etc., due to chronic thrombosis of the aortic bifurcation); in the other 7 the resection was carried out for aneurysm of the abdominal aorta.

The grafts used in all patients were acquired from the bodies of young adults, by sterile technique, shortly after death. After appropriate cultures were taken, the graft was placed in a glass tube and quickly frozen in a dry ice-alcohol mixture at −78° C. The storage temperature was also −78° C. When the graft was to be used, it was quickly thawed by placing it in saline at +38° C. None of the patients was heparinized after operation, but regional heparinization of the lower extremities was carried out during the time that the blood flow was interrupted. The actual surgical procedure was very simple, consisting of resection of the involved area and simple end-to-end anastomosis between the graft and the aorta and common iliac arteries. Twelve of the 14 patients had good or excellent results; one patient was unimproved and one died. Of the 14 patients, pulses were restored bilaterally in 10, while in 4 the restoration was unilateral.

It is concluded that resection of the abdominal aorta for aneurysm or Leriche's syndrome is a safe and practical procedure. S. J. SHANE

Cardiovascular and Blood Volume Alterations Resulting from Intrajejunal Administration of Hypertonic Solutions to Gastrectomized Patients: The Relationship of these Changes to the Dumping Syndrome.

ROBERTS, K. E. *et al.*: ANN. SURG., 140: 631, 1954.

The dumping syndrome is defined as a fullness or churning in the epigastrium followed by weakness, sweating, tachycardia, tachypnœa, pallor and an elevated blood pressure occurring in gastrectomized patients 15 to 20 minutes after the ingestion of food. A group of 21 patients, of whom 10 had undergone total gastrectomy, 4 subtotal gastrectomy, and one jejunostomy, while 6 had an intact stomach, were studied. Serial electrocardiograms were taken, plasma volume and hæmatocrit determined and other chemical analyses made after test meals and use of hypertonic solutions. It was shown that intrajejunal administration of hypertonic solution or starch causes an acute decrease in circulating blood volume resulting from a shift of plasma water into the intestinal lumen. Differences in isomolarity between the administered solution and the plasma cause this shift of

fluid. Symptoms and electrocardiographic changes typical of the dumping syndrome coincide with the decrease in blood volume. Similar alterations occur in patients with an intact stomach when hypertonic solutions are administered. BURNS PLEWES

Dupuytren's Contracture: The Significance of Various Factors in its Etiology.

GORDON, S.: ANN. SURG., 140: 683, 1954.

In an attempt to relate various factors and diseases to the etiology of Dupuytren's contracture, 2,705 patients in various Ontario hospitals were examined. An incidence of 13.6% (369 cases) was found. The greatest number were between 55 and 75 years of age. No statistically significant difference was demonstrated between the sexes. Occupation was not of importance. Arthritis, diabetes and epilepsy could not be implicated. Patients hospitalized for tuberculosis showed a greater incidence. Dupuytren's contracture remains a definite clinical entity of unknown etiology. BURNS PLEWES

OBSTETRICS AND GYNÆCOLOGY

Stilbœstrol-induced Hyperhormonal Amenorrhœa for the Treatment of Pelvic Endometriosis.

HASKINS, A. L. AND WOOLF, R. B.: OBST. & GYNEC., 5: 113, 1955.

Fifteen patients with symptomatic pelvic endometriosis were treated for this condition with massive doses of stilbœstrol for an average of 190 treatment days. All patients were asymptomatic during the treatment.

After the treatment was discontinued, symptoms recurred in four patients, the earliest immediately after treatment was completed and the latest 38 months after therapy. Eleven patients have remained asymptomatic in an average follow-up period of 21 months. No serious complications of therapy were encountered.

The size and locations of the aberrant endometrial tissue did not change materially during therapy or thereafter. Pain and tenderness in the involved areas underwent a dramatic remission shortly after the initiation of the stilbœstrol therapy. Endometrial biopsies taken during the course of therapy revealed only hyperplasia.

Stilbœstrol-induced hyperhormonal amenorrhœa compares favourably with pregnancy for the treatment of pelvic endometriosis. It may be used readily when pregnancy is not advisable and prior to, or as a substitute for, surgical procedures in the treatment of pelvic endometriosis. ROSS MITCHELL

Intrauterine and Neonatal Pneumonia.

PENNER, D. W. AND MCINNIS, A. C.: AM. J. OBST. & GYNEC., 69: 147, 1955.

Seventy-one cases are summarized. These constituted 11% of all intrauterine and neonatal deaths autopsied at the Winnipeg General Hospital between January 1940 and December 1951. In most cases positive cultures were obtained or bacteria were found in the tissue section of the lungs. The control series also had a relatively high incidence of positive cultures but bacteria were seldom found in the tissue sections of the lungs. Interpretation of bacteriological findings must therefore be made with caution.

Most pneumonias are of a diffuse bilateral, predominantly polymorphonuclear leukocytic type. Amniotic fluid content in the lungs does not appear to be a very significant etiological factor. The highest incidence of pneumonia occurs in premature infants with early rupture of the membranes. Recognition of the following facts might reduce the incidence of intrauterine pneumonia: (a) Since vaginal examination before delivery may infect both mother and infant, this should be done only when strictly indicated and then under aseptic technique. (b) Artificial rupture of the membranes should be restricted to cases where there is a definite indication. (c) When there is early rupture of the membranes, antibiotics should be given to the mother. (d) Mouth-to-mouth resuscitation is a hazardous procedure. ROSS MITCHELL

Intrauterine Roentgenography as an Aid in Determining Fetal Age.

ADAMS, T. W.: OBST. & GYNEC., 5: 43, 1955.

In those cases in which pre- and post-delivery x-rays were taken at a sufficiently close interval of time to make comparison possible, the interpretation of the intrauterine roentgenograms proved to be 89% accurate. It is believed, consequently, that technically visualization of the distal epiphysis of the femur can be carried out with a low degree of error.

The appearance of ossification was awaited in 55 cases before birth was accomplished. Among these there were two fetal deaths; one occurred in a severe Class D diabetic, and at autopsy death was ascribed to a diabetic syndrome. In the other the appearance of the epiphysis was somewhat doubtful, and death was ascribed to diabetes and secondary pneumonia. In this group there was no fetal mortality from prematurity.

Eight patients were delivered before the appearance of ossification of the distal femoral epiphysis and four fetal deaths resulted. Of these one was a stillbirth, in a severe Class D diabetic, one died of prematurity alone, one of prematurity and diabetic syndrome and one of prematurity and erythroblastosis. All the remaining four were definitely premature and survived only with adequate premature care and protracted incubation.

No claim is made that the procedure is completely reliable; undoubtedly fetal survival can occur in the absence of epiphyseal ossification and, conversely, fetal death may result despite its presence. However, it is felt that the procedure constitutes another and possibly more individually accurate method of determining the time during pregnancy when the induction of labour may be undertaken with a comparatively good outlook for fetal survival. ROSS MITCHELL

RADIOLOGY

Total Myelography.

BRIERRE, J. T. AND COLCLOUGH, J. A.: RADIOLOGY, 64: 81, 1955.

The authors describe a technique for the examination of the spinal subarachnoid space in cervical, dorsal and lumbar regions. The spinal puncture is done in an area remote from the suspected lesion. After removal of spinal fluid, 21 c.c. of Pantopaque is injected into the subarachnoid space. The needle is withdrawn and the patient straightens out and lies prone. The lumbosacral region is observed in the vertical position. The dorsal area is examined by lowering the table to the horizontal position and having the patient lie supine. The cervical region is visualized by putting the patient in the prone position and lowering the head of the table to about 45° tilt. The following features are worthy of note: (1) The method reduces x-ray exposure and effort on the part of the radiologist and surgeon. (2) In the erect position 21 c.c. of Pantopaque fills the distal subarachnoid space from the sacral cul-de-sac to the first lumbar or in some cases as high as the 11th dorsal spine, making the examination of the lumbar area easy and accurate. (3)

Canad. M. A. J.
May 15, 1955, vol. 72

It allows examination of thoracic and cervical areas without excessive inversion of the patient. (4) Removal of the oil is easier and there is less globulation. (5) The authors state that the method gives very accurate results in their experience in all areas.

CHARLES E. VAUGHAN

Bronchiectasis—Dextrocardia—Sinusitis: A Contribution to the Etiology of Bronchiectasis.

GUDBJERG, C. E.: ACTA RADIOLOGICA, 42: 413, 1954.

Bronchiectasis has been known as a well-defined disease entity for more than a century; classically, it is divided into congenital and acquired. On the basis of radiological, clinical and experimental studies the development of acquired bronchiectasis is explained by complete or partial bronchial obstruction by a foreign body, a tumour or inflammatory products which in turn causes a retention of bronchial secretion. Owing to secondary infection a chronic inflammatory reaction develops in the bronchial wall which becomes weakened. The increase in intrabronchial pressure produced by cough will then give rise to dilatation of the bronchi. Atelectasis in children, and other primary diseases commonly found in the history of bronchiectasis, are caused without exception by an inflammatory condition in the lung. Bronchial exudate and inflammatory swelling of the bronchial mucosa may close the bronchial lumen and cause bronchiectasis. The authors believe therefore that bronchiectasis is in all probability invariably acquired.

Obstruction and infection are considered to be the most common causes of the disease, but compression by enlarged lymph nodes and traction from surrounding pulmonary tissue may also produce bronchial dilatations. Definite hereditary facts have never been demonstrated. In 25 patients with dextrocardia not a single case of bronchiectasis was found. Among 35 patients with bronchiectasis confirmed by bronchography, sinusitis was demonstrated in 28.6% by combined radiological and otolaryngological examinations. CHARLES E. VAUGHAN

THERAPEUTICS

Ulcerative Colitis: Therapeutic Effects of Corticotropin (ACTH) and Cortisone in 120 Patients.

KIRSNER, J. B. AND PALMER, W. L.: ANN. INT. MED., 41: 232, 1954.

Corticotropin (ACTH) or cortisone was administered to 120 patients with moderately severe or severe ulcerative colitis. The initial doses were, for ACTH, 30 i.u. intramuscularly every six hours (120 units per day) and for cortisone, 200 or 300 mgm. by mouth daily. The immediate clinical response to corticotropin was judged as good or favourable in 94 of the 108 ACTH patients, and in nine of the 12 cortisone patients. The response included the prompt subsidence of fever, tachycardia, abdominal distress and bloody diarrhœa, and increased appetite and a pronounced sense of well-being. The proctoscopic appearance of the bowel improved in the vast majority of this group. Eosinophil counts decreased significantly in 67 of the 72 patients examined. Alkalosis occurred in 76 of the 102 patients whose electrolytes were measured repeatedly; hyperglycæmia in eight of 43 patients; glycosuria in 25 of 99 patients, and leukocytosis in 62 of 92 patients. Œdema developed temporarily in 102 patients, rounding of the face in 81, acne in 69 and hypertension in 35. Eight patients developed allergy to ACTH. Infections complicated therapy in 16 instances.

Symptoms have recurred thus far in 68 of the 94 patients responding initially to ACTH, and in six of the nine cortisone-treated cases improving immediately. Many of the recurrences appeared to be less severe than those preceding steroid therapy and have subsided with careful medical management; some of these recurrences were, in fact, relapses soon after the termination of therapy. Remissions have continued in 26 of the 94 patients in the ACTH group and in three of the nine in the cortisone group responding immediately; nine patients have remained well for two and three years after treatment. Numerous additional patients, experiencing recurrences shortly after treatment, subsequently have remained well for long periods. Corticotropin gel, though less potent than the aqueous preparation, was clinically effective in occasional patients. Corticotropin intravenously induced striking and, at times, dramatic improvement in the 14 patients not responding adequately to ACTH intramuscularly. Compound F, administered orally in moderate amounts to three patients, appeared to be less effective than ACTH and more potent than cortisone.

The current clinical status seems excellent in 35 patients and moderately improved in 57; 12 are unimproved, but continue medical treatment; nine patients required colectomy and ileostomy, with excellent to satisfactory results in seven. There were seven deaths, four of causes unrelated to steroid therapy and three probably attributable to the use of corticotropin. In the entire series of 120 patients, medical treatment controlled symptoms effectively in 77%; 10% were unimproved but continue therapy; 7% required surgery, and 6% died. S. J. SHANE

The Adverse Effects of Belladonna Alkaloids in Benign Pyloric Obstruction.

KRAMER, P.: NEW ENGLAND J. MED., 251: 600, 1954.

The belladonna alkaloids are widely employed in the therapy of peptic ulcer, particularly when there is delayed gastric emptying. While their cholinergic activity may tend to relax spasm at the pylorus, this may be more than counterbalanced by decreased gastric tone and motility.

A group of 15 patients with pyloric obstruction of varying degree, complicating chronic peptic ulcer, were studied following ingestion of barium, with and without preliminary administration of one of the belladonna alkaloids. In nine patients the drugs produced or increased gastric retention and in four patients this retention was complete after five hours.

While the belladonna alkaloids may be of value in diminishing gastric secretion, the fact that they may aggravate pyloric obstruction demands caution in their use in patients with benign pyloric obstruction of any degree. NORMAN S. SKINNER

PUBLIC HEALTH

A Poisoning Control Programme.

PRESS, E. AND MELLINS, R. B.: AM. J. PUB. HEALTH, 44: 1515, 1954.

Toxic products now synthesized by modern industry for household purposes are available for use and deadly misuse in almost every home. Thus, poisoning now looms as a major public health problem. The epidemiological approach, which has proved its value in solving other public health problems, can be applied effectively to the public health problem of poisoning, as the Chicago Poisoning Control Programme shows.

In 1950 the American Academy of Pediatrics, concerned about the increasing incidence of accidental

injury and poisoning, appointed a nation-wide Committee on Accident Prevention. Arising from this, a Poisoning Control Committee was formed in Chicago in the fall of 1952 under the chairmanship of Dr. Edward Press, and consisting of the chairman of the department of Pædiatrics in each of the five medical schools of Chicago and in a local medical centre with a separate children's hospital; the state chairman of the Academy of Pædiatrics; and representatives of the City Board of Health, the State Toxicological Laboratory, the American Medical Association, the Federal Food and Drugs Administration, and the National Safety Council.

A loose-leaf reference guide to the toxic constituents of household substances, together with an outline of recommended treatment following the ingestion of these substances, was prepared by the committee. This guide was used as the basis of treatment in the emergency rooms of the hospitals with which the pædiatric members of the committee were affiliated. In each of the six hospitals the responsible physician was at liberty to modify the suggested treatment, but the data on all cases treated were reported to the Chicago Board of Health. The reports were analysed and summarized by members of the health department with the guidance of committee members. Mechanical tabulation was used to facilitate analysis, and the information was made available periodically to the participating centres. Requests from doctors for information about treatment were referred to the committee member or his alternate at any of the participating hospitals, to the Chicago Board of Health, or to the committee chairman. The State Toxicological Laboratory in Chicago analysed gastric washings, body fluids and other specimens. The City Board of Health Laboratory provided facilities for the analysis of specimens for lead content.

Three hundred and seventy-five patients received emergency treatment for swallowing household substances. Aspirin, kerosene and other petroleum distillates, bleach, insecticides, and rodenticides have been among the commonest substances swallowed by children. Proportionately more patients in the lower economic groups were involved. In the series of 375 cases, no death was reported, although one occurred; this was due to the swallowing of turpentine and was found in a routine screening of all death certificates in the city. Two more deaths in the participating hospitals did not follow an acute episode of poisoning but resulted from the chewing of paint peelings over many days. Follow-up home visits or telephone calls were made by Board of Health personnel to help correct the conditions leading to the accidental swallowing of the poisonous substance, and to confirm details of treatment and results.

After a trial period from November 15, 1953, to March 10, 1954, the committee agreed that the programme should be expanded to include other hospitals wishing to participate. The Chicago Medical Society and the Chicago Pediatric Society endorsed the programme. Twenty hospitals are now participating, and the programme has extended from the city to neighbouring areas, with the inclusion of three more full-time health departments.

A co-ordinated poisoning control programme has distinct advantages over individual efforts by hospitals, medical centres and medical colleges. In addition to more direct preventive and treatment services, the benefits include continuous and co-ordinated professional and lay education. The programme also affords possibilities for research, including evaluation of the results from different methods of treatment. The findings can be helpful, too, in providing a sound basis for the revision of legislation governing labelling and other safeguards. R.R.

FORTHCOMING MEETINGS

CANADA

BRITISH COMMONWEALTH MEDICAL CONFERENCE OF THE BRITISH MEDICAL ASSOCIATION, Toronto, Ontario. (Dr. A. D. Kelly, Canadian Medical Association, 244 St. George Street, Toronto 5.) June 14-16, 1955.

CANADIAN SOCIETY OF MICROBIOLOGISTS—5th Annual Meeting, Winnipeg, Man. (University of Manitoba, Winnipeg, Man.) June 15-17, 1955.

COMBINED MEETING OF THE CANADIAN PÆDIATRIC SOCIETY, SOCIÉTÉ CANADIENNE DE PÉDIATRIE, BRITISH PÆDIATRIC ASSOCIATION, AMERICAN PÆDIATRIC SOCIETY AND THE SOCIETY FOR PÆDIATRIC RESEARCH, Quebec City, Quebec. (Dr. J. C. Rathbun, Secretary-Treasurer, 526 Waterloo Street, London, Ont.) June 15-18, 1955.

BRITISH MEDICAL ASSOCIATION, CANADIAN MEDICAL ASSOCIATION, ONTARIO MEDICAL ASSOCIATION, Conjoint Meeting, Toronto, Ont. (Dr. A. D. Kelly, General Secretary, Canadian Medical Association, 244 St. George Street, Toronto 5, Ont.) June 17-24, 1955. (Scientific Sessions June 20-24.)

CANADIAN UROLOGICAL ASSOCIATION, Annual Meeting, King Edward Hotel, Toronto. (Dr. David Swartz, Secretary, Canadian Urological Association, 322 Medical Arts Bldg., Winnipeg.) June 20-22, 1955.

CANADIAN ACADEMY OF ALLERGY, Annual Meeting, Royal York Hotel, Toronto, Ont. (Dr. P. A. Ryan, Acting Secretary, 229 St. Clair Avenue West, Toronto 7, Ont.) June 21, 1955.

CANADIAN PUBLIC HEALTH ASSOCIATION AND ALBERTA PUBLIC HEALTH ASSOCIATION, Conjoint Meeting, Edmonton, Alta. (Dr. William Mosley, Honorary Secretary, 150 College Street, Toronto 5, Ont.) September 6-8, 1955.

UNITED STATES

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, Monterey Lodge, Monterey, California. (Dr. John A. Taylor, Secretary, 2 East 54th Street, New York 22, N.Y.) May 22-25, 1955.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Statler Hotel, Detroit. (Dr. Lloyd N. Yepsen, Secretary, New Lisbon, N.J.) May 24-28, 1955.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Atlantic City, N.Y. (Mr. Murray Kornfeld, Executive Director, 112 East Chesnut St., Chicago 11, Illinois.) June 2-5, 1955.

EIGHTH ANNUAL INDUSTRIAL MICROBIOLOGY INSTITUTE, West Lafayette, Indiana. (Dr. C. L. Porter, Director of the Institute, Department of Biological Sciences, Purdue University, West Lafayette, Indiana.) June 5-11, 1955.

AMERICAN MEDICAL ASSOCIATION, 1955 Annual Meeting, Atlantic City, N.J. (Dr. George F. Lull, Secretary, 535 North Dearborn Street, Chicago 10, Ill.) June 6-10, 1955.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, 9th Annual Meeting, Palmer House, Chicago, Illinois. (Dr. W. T. Liberson, Secretary, Veterans' Administration Hospital, Northampton, Mass.) June 10-12, 1955.

ANNUAL ASSEMBLY IN OTOLARYNGOLOGY, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois. (Dr. F. L. Lederer, Professor and Head of the Department.) September 19-October 1, 1955.

ANNUAL MEETING OF THE AMERICAN ACADEMY FOR CEREBRAL PALSY, Memphis, Tennessee. (Dr. R. A. Knight, Secretary-Treasurer, 869 Madison Avenue, Memphis 3, Tenn.) October 10-12, 1955.

Canad. M. A. J.
May 15, 1955, vol. 72

AMERICAN HEART ASSOCIATION, Annual Meeting and Twenty-Eighth Annual Scientific Session, Jung Hotel, New Orleans, Louisiana. (The Medical Director, American Heart Association, 44 East 23rd Street, New York 10, N.Y.) October 22-26, 1955.

AMERICAN PUBLIC HEALTH ASSOCIATION, INC., 83rd Annual Meeting and Meetings of Related Organizations, Kansas City, Missouri. (The American Public Health Association, Inc., 1790 Broadway, New York 19, N.Y.) November 14-18, 1955.

OTHER COUNTRIES

FIFTEENTH CONGRESS OF FRENCH-SPEAKING PÆDIATRICIANS, Marseilles, France. (Dr. Réné Bernard, Clinique Médicale Infantile, Hôpital de la Conception, Marseilles.) May 23-25, 1955.

INTERNATIONAL COLLEGE OF SURGEONS—20th Anniversary Meeting, Geneva, Switzerland. (Dr. Max Thorek, 850 West Irving Park Road, Chicago 13, Ill.) May 23-26, 1955.

SEVENTH INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Lausanne, Switzerland. (Prof. Hauduroy, 19 avenue César-Roux, Lausanne.) May 26-31, 1955.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland. (Capt. J. E. Stone, Hon. Secretary, International Hospital Federation, 10 Old Jewry, London, E.C.2, England.) May 29-June 3, 1955.

EUROPEAN CONGRESS ON RHEUMATISM, Scheveningen, The Hague, Netherlands. (Dr. H. van Swaay, Secretary, Pieter Bothstraat 12, The Hague, Netherlands.) June 13-17, 1955.

FIFTH CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Stockholm, Sweden. (Dr. J. M. Lemoine, 187 boulevard Saint-Germain, Paris 7e.) June 18-19, 1955.

FOURTH COMMONWEALTH HEALTH AND TUBERCULOSIS CONFERENCE, Royal Festival Hall, London, England. (Secretary-General, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1, England.) June 21-25, 1955.

JOURNÉES MÉDICALES DE FRANCE ET DE L'UNION FRANÇAIS, Strasbourg, France. (Dr. L. Michelet, 12, rue Pierre-Geofroix, Colombes (Seine).) June 1955.

2E RÉUNION SYNDICALE INTERNATIONALE DES GYNÉCOLOGUES ET OBSTÉTRICIENS, l'Hôtel des Syndicats Médicaux, Paris, France. (Dr. Jacques Courtois, 1, rue Racine, Saint Germain-en-Laye, Seine-et-Oise.) June 27-28, 1955.

SECOND CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Cambridge, England. (Organizing Secretary, Mr. J. G. L. Jackson, Congress Office, 152 Harley Street, London, W. 1, England.) July 4-8, 1955.

CONGRESS OF INTERNATIONAL ASSOCIATION OF APPLIED PSYCHOLOGY, London, England. (Dr. C. B. Frisby, President, National Institute of Industrial Psychology, 14 Welbeck Street, London, England.) July 18-23, 1955.

SIXTEENTH CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Copenhagen, Denmark. (Dr. Hasner, 7 Blegdamsvej, Copenhagen.) July 24-31, 1955.

SIXTH INTERNATIONAL ANATOMICAL CONGRESS, Paris, France. (Prof. Gaston Cordier, Secretary-General, 45 rue des Saints-Pères, Paris 6e, France.) July 25-30, 1955.

FOURTEENTH BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY, Oxford, England. (The Secretary, 14th British Congress of Obst. and Gyn., Maternity Dept., Radcliffe Infirmary, Oxford.) July 27-30, 1955.

THIRD INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Brussels, Belgium. (Prof. C. Liébecq, Secretary-General, 17 Place Delcour, Liège, Belgium.) August 1-6, 1955.

INTERNATIONAL CONGRESS OF PLASTIC SURGERY, Stockholm and Uppsala, Sweden. (Dr. Tord Skoog, General Secretary, Uppsala University, Sweden.) Stockholm, August 1-4, and Uppsala, August 5, 1955.

NEWS ITEMS

SASKATCHEWAN

The University of Saskatchewan at Saskatoon conferred seven honorary Doctor of Laws degrees in a special convocation on Saturday, May 14, the day following the regular convocation. This special convocation was held in conjunction with the official opening of the new University Hospital. These degrees were conferred upon the following: Dr. G. Harvey Agnew of Toronto, Professor of Hospital Administration, University of Toronto; Dr. Edward J. Baldes of Rochester, Minnesota, Professor of Biophysics, Mayo Foundation; Dr. R. D. Defries of Toronto, Director of the School of Hygiene and Director of the Connaught Medical Research Laboratories, University of Toronto; Kathleen W. Ellis of Penticton, B.C., formerly Director of the School of Nursing and Professor of Nursing, University of Saskatchewan, and former Director of Nursing Services, Vancouver General and Winnipeg General Hospitals; Dr. W. S. Lindsay, Dean Emeritus of the College of Medicine, University of Saskatchewan, and Secretary of the University Hospital Board; Dr. F. D. Mott of Washington, D.C., Medical Administrator, Memorial Hospital Association, and former Deputy Minister of Public Health for Saskatchewan; Dr. J. B. Ritchie of Regina, Saskatchewan, a member of the Council of the College of Physicians and Surgeons of Saskatchewan and a former President of the College of Physicians and Surgeons of this province.

A symposium on The Hospital in Tomorrow's World was the first event on May 14 when the University Hospital, Saskatoon, was officially opened. The following topics were presented:

The Background of the University Medical Centre. W. S. Lindsay, Dean Emeritus of Medicine, University of Saskatchewan, and Secretary of the University Hospital Board.

The University Hospital and Clinical Investigation. J. S. L. Browne, Professor of Medicine, McGill University, and Director of the University Clinic, Royal Victoria Hospital, Montreal.

The Social Sciences and Improvement of Patient Care. Esther Lucile Brown, Executive Staff, Russell Sage Foundation, New York.

Next Steps in Saskatchewan's Health Service — Strengthening the Quality of Medical and Hospital Care. Frederick D. Mott, Medical Administrator, Memorial Hospital Association, and Senior Medical Consultant, United Mine Workers of America Welfare and Retirement Fund, Washington, D.C.

The Teaching Clinic and Tomorrow's Doctor. James Howard Means, Jackson Professor of Medicine Emeritus, Harvard Medical School; Acting Medical Director, Massachusetts Institute of Technology, Cambridge, Mass.

The convocation address was delivered by Dr. G. Harvey Agnew, Professor of Hospital Administration, University of Toronto.

One of the first departments to reach full strength at the College of Medicine and University Hospital will be Anæsthesia. Under the chairmanship of Dr. Gordon M. Wyant a team of three "geographical" full-time anæsthetists will be joined by part-time teachers from the other hospitals. Dr. Allen B. Dobkin will come as assistant professor in July from a senior instructorship at Western Reserve University, Cleveland. Dr. Christopher J. Kilduff, graduate of the National University of Ireland, and now resident at the University Hospital, will become instructor in July.

Dr. Wyant was assistant professor at the University of Illinois for three years before becoming professor and head of the department at Loyola University and chief of anæsthesia at Mercy Hospital, Chicago, in 1953. Born

and educated in Germany, Dr. Wyant graduated in medicine at Bologna and continued his studies at Birmingham and London. For four years he served in the Royal Army Medical Corps as a specialist in anæsthesia. His research work and publications have been along both clinical and pharmacological lines, and for three years he has been consultant to the Council of Pharmacy and Chemistry of the American Medical Association.

After graduating from the University of Toronto in Arts and Medicine, Dr. Dobkin spent a year in pathology at the Banting Institute before taking extensive training in anæsthesia in Cleveland and Minneapolis. Last year, while holding a National Research Council Fellowship in the graduate school at McGill, he studied hibernating drugs in the treatment of shock. His publications cover a wide range of interest in basic problems in the physiology and pharmacology of anæsthesia.

During the week of May 8 Dr. G. E. Fryer and Dr. F. C. Pace addressed the members of the District Medical Societies of Saskatoon, Rosetown, Regina, Prince Albert and Moose Jaw, presenting a symposium dealing with both the health and the special weapons aspects of civil defence. Dr. Fryer has been associated with the Department of Veterans Affairs and with the Department of National Health and Welfare, Civil Defence Health Services, since the end of the last war. Dr. Pace is medical consultant, Special Weapons Section, Civil Defence Health Services, Ottawa, and secretary of the D.M.R.A.C. panel on radiation protection and treatment. He is also special lecturer to the Faculty of Medicine, University of Toronto.

Among the highlights of the last provincial budget was that public health expenditures will be increased by two million dollars to reach $22,174,250, providing for the opening of the University Hospital and improved psychiatric services.

G. W. PEACOCK

NEW BRUNSWICK

Dr. J. A. MacDougall of Saint John was elected chairman of the Maritime Hospital Service Association at the annual meeting in Moncton. Dr. MacDougall is also vice-president of the National Council of Blue Cross Plans for Canada.

The March meeting of the Saint John Medical Society was held in the auditorium of the Pathological Building of the General Hospital. Dr. Fred Cheesman presided. Three distinguished lawyers, Mr. A. B. Gilbert, Q.C., Mr. B. R. Guss, Q.C., and Mr. Paul Barry, Q.C., representing the local, provincial and Canadian Bar associations, addressed the large audience on the theme "A better understanding between the legal and medical professions," touching on various aspects of legal practice as it affected citizens and especially doctors. The doctors present felt that further meetings on common ground would be to the advantage of both professional groups.

Dr. J. A. M. Bell of Fredericton, director of the New Brunswick Poliomyelitis Clinic at the Victoria Public Hospital, has welcomed the first ten patients into the nearly completed new building, which will house the many facilities required for the care of poliomyelitis patients. Dr. A. F. Torrie is orthopædic surgeon in this department.

Dr. A. F. Crook, F.R.C.S.(Edin.), D.M.R.T., has joined the radiological staff of the Saint John General Hospital as assistant radiotherapist.

Influenza has been so prevalent in lower New Brunswick that Dr. F. C. Hazen, Local Officer of Health in Saint John, has prohibited visiting by the general public in the city hospitals.

Dr. C. R. Trask, director of the Saint John General Hospital, has been elected a member of the Society of Medical Administrators.

The New Brunswick Department of Health has begun the immunization of schoolchildren in grades 1 and 2 with the Salk poliomyelitis vaccine. The children will receive two inoculations with a short interval, to be followed by a booster inoculation in about seven months. The project is under the control of Dr. A. F. Chaisson, director of the Division of Communicable Diseases.

Dr. G. E. Maddison, Director of Tuberculosis Control for New Brunswick, announces that the 1954 tuberculosis death rate for the Province has been tentatively set at 8.8 per 100,000 population. The rate is a reduction from the previous low of 12.9 per 100,000.

Dr. W. D. Miller was the chairman of a committee composed of Dr. A. L. Donovan, Dr. J. A. Finley, and Dr. F. L. Whitehead who organized and guided the spring clinical session of the Saint John Medical Society, held in the Pathological Institute of the Saint John General Hospital and the D.V.A. Hospital in Lancaster. Dr. Campbell McG. Gardner, Associate Professor of Surgery, McGill University, and Surgeon-in-Chief of Queen Mary Veterans Hospital, Montreal, presented two clinical lectures, "Difficulties of interpretation of the results of gastric operations with particular reference to the post-gastrectomy syndrome" and "Ulcerative colitis." He also was the speaker at the evening dinner meeting, when his subject was "The medical horizon." Dr. Earl E. Ewart, senior urologist of the Lahey Clinic, Boston, gave three papers: "Experiences with two million supervoltage rotational therapy in treatment of carcinoma of the bladder," "Diagnosis and treatment of renal tumours," and "Unrecognized prostatism." Six papers were presented by local physicians: "Practical aspects of antibiotic therapy," Dr. K. J. Rodger; "Poliomyelitis vaccinations," Dr. A. E. Chaisson; "Early treatment of burns and some practical aspects of shock and electrolyte balance," Dr. T. E. Grant and Dr. J. A. MacDougall; "The use and misuse of metals in surgery," Dr. P. G. Laing; "Some aspects of trauma," Dr. R. B. Eaton and Dr. D. A. Thompson; and "Malar bone fractures involving the orbit," Dr. G. C. Gaulton. The attendance at this third annual spring conference was most satisfactory. The generosity of our visiting speakers and the interest and enthusiasm of the local doctors in presenting papers and in providing discussions made the meeting a successful enterprise in our medical society's effort to acquaint the physicians practising in the province with current advances, without requiring too long an absence from their practice.

A. S. KIRKLAND

NOVA SCOTIA

In March the New Aberdeen Hospital was opened in New Glasgow. Situated on a fine spacious site on the East River Road, it represents the effort and enterprise of the populous eastern section of the County of Pictou. It will replace the old hospital of the same name on the west side of New Glasgow, opened in 1897.

The new building, opened by Harold Connolly, M.L.A., has a capacity of some 200 beds and its design is completely modern. Dr. Hugh MacKay of New Glasgow will be its medical director and Miss Mary Ross, R.N., its superintendent of nurses. For several years the hospital facilities in this area have been taxed to capacity and the relief from a state bordering on crowding will be welcomed by patients as well as by the medical and nursing staffs. Working under such improved con-

Canad. M. A. J.
May 15, 1955, vol. 72

ditions will prove a source of genuine inspiration to all concerned with the care of the sick.

Dr. H. B. Atlee, Professor of Obstetrics and Gynæcology, Dalhousie University, recently was guest speaker at the refresher course in obstetrics and pædiatrics of the University of Saskatchewan. On his way to the West he spoke to the Hamilton Academy of Medicine on "Natural Childbirth" and addressed the medical students of the University of Western Ontario.

Dr. Joseph Edward Stapleton, of Sydney, Australia, arrived in Halifax in January to accept an appointment as chief of radiation therapy at the Victoria General Hospital, and Associate Professor of Radiology in Dalhousie University. Just prior to his new appointment Dr. Stapleton practised in Regina, Saskatchewan, where he was a senior member on the staff of the Allan Blair Cancer Clinic. A graduate of Sydney University, he was in private specialist practice in Sydney, and later a staff member of the Holt Radium and Cancer Institute in Manchester, England, in 1948. Two years later, after further postgraduate qualification, Dr. Stapleton was appointed to the staff of the Royal Cancer Hospital in London, England. In 1952, he established the isotope department of the M. D. Anderson Hospital at the University of Texas. Later, as a Bertner Fellow, he visited and studied in major cancer centres in the United States.

Dr. S. W. Williamson of Yarmouth, who recently celebrated his 86th birthday, has been receiving best wishes from his many friends. He has been in practice for a period of 59 years. In January he joined the many on Lake Mill to enjoy an afternoon of skating.

The establishment by some 26 organizations and agencies of a rehabilitation centre on the ground floor of the Halifax Infectious Diseases Hospital has been recommended by the Executive Committee and Health Commission of the City of Halifax.

The proposal has been that the city move its infectious cases to the second floor of the hospital and build a ramp connecting the second floor with the corresponding floor of the Tuberculosis Hospital. The city would then turn over the ground floor of the hospital to the Rehabilitation Council.

Three thousand young Halifax schoolchildren are officially "Polio Pioneers" after receiving their official membership cards and "pioneer" buttons from the City Health Department. The youngsters, members of kindergarten and grades one and two of all city schools, were vaccinated with either Salk vaccine or a harmless serum in tests in June last year. They were among 55,000 schoolchildren across Canada who participated in the tests last year.

For the second time in six months, personnel at H.M.C.S. *Stadacona*, the Navy's big Halifax training base, established a nationwide record for the number of donations at a single blood donor clinic during a three-day effort.

The clinic, which was intended as a two-day affair, established a new national mark of 1,080 donors. This is four above the existing record, also set by the sailors at *Stadacona* during a clinic held last August.

The big reason for the two concentrated drives to obtain blood for the Red Cross Blood Transfusion Service has been friendly rivalry with the Navy's basic training base, H.M.C.S. *Cornwallis*, at Deep Brook. Cornwallis sailors donated 1,076 pints of blood during a clinic last spring and the Stadacona tars have made a determined—and successful—effort to go over that mark.

C. M. HARLOW

NEWS OF THE ARMED FORCES

Surg. Lt. Cdr. J. S. Simpson, R.C.N., has been appointed from the R.C.N. Hospital, Esquimalt, as principal medical officer to the cruiser *Ontario*. He replaced Surg. Cdr. J. W. Green, R.C.N., who has been appointed anæsthetist to the R.C.N. Hospital, Esquimalt.

Surg. Lt. Cdr. D. V. Willoughby, R.C.N., has begun postgraduate training in surgery at the University of Toronto.

Surg. Lt. N. W. Bradford, R.C.N., has been appointed from the carrier *Magnificent* to the U.S.N. School of Aviation Medicine, Pensacola, Florida, for a course. He will be relieved in the *Magnificent* by Surg. Lt. E. R. Keirstead, R.C.N., who has completed a similar course.

Colonel R. J. Nodwell, C.D., M.D., Deputy Director General of Medical Services (Army), Colonel S. G. U. Shier, O.B.E., C.D., M.D., Command Medical Officer, Central Command, and Colonel E. J. Young, C.D., M.D., D.P.H., who recently vacated the appointment of A.D.M.S. 1 Commonwealth Division in Korea, attended a symposium on the management of mass casualties, conducted at the Walter Reed Army Medical Center, Washington, D.C., from March 7 to 16.

Major R. Fournier, M.D., B.M., D.P.H., has been posted from the appointment of Command Hygiene Officer, Quebec Command, to the Canadian Military Truce Teams in Indo-China. While in Indo-China, he will be responsible for the supervision of the medical attention afforded Canadian personnel on the truce teams. Major K. D. McQuaig, B.A., M.D., C.M., D.P.H., has recently returned to Canada from service as medical officer with the truce teams.

Major J. E. Gilbert, M.D., B.Sc., M.R.C.S., L.R.C.P., D.R.C.O.G., attended the joint spring meeting of the Commission on Enteric Infections held in New Orleans between March 23 and 25. Major Gilbert contributed to the discussions on Arctic sanitation.

Lt.-Col. W. R. I. Slack, C.D., of the Medical Directorate, Army Headquarters, attended the 23rd Annual Venereal Disease Conference, sponsored jointly by the United States Public Health Service and the Division of Graduate Medicine, Tulane University.

Promotions

Captain D. E. Yates, M.R.C.S., L.R.C.P., M.B., B.S., Winnipeg Stations Hospital, has been promoted to the rank of Major.

Captain D. G. Guthrie, B.Sc., M.D., C.M., has been promoted to acting Major. He will continue in his employment as radiologist at Kingston Military Hospital.

Wing Cdr. H. B. Hay, D.S.O., D.F.C., C.D., Staff Officer Medical Services R.A.F. at Canadian Joint Staff, London, attended the meeting of the International Civil Aviation Organization in Paris beginning April 25, in company with other Canadian representatives. The purpose of the meeting was to discuss hearing requirements for flight crew members.

Air Commodore A. A. G. Corbet, E.D., C.D., Q.H.P., Director General Medical Services (Air), was an examiner for the American Board of Preventive Medicine at the examinations for the certification of specialists in Aviation Medicine, held March 17-19 in Washington, D.C.

BOOK REVIEWS

THE HISTORY AND CONQUEST OF COMMON DISEASES

Edited by W. R. Bett, Research Librarian of the National Association for the Prevention of Tuberculosis, in London. 334 pp. $5.25. University of Oklahoma Press, Norman; Burns & MacEachern, Toronto 2, 1954.

Twenty years ago a *Short History of Some Common Diseases* was published, "mainly for students and practitioners, and possibly also for patients." Dr. Bett has completely re-cast this work with the help of a team of notable contributors from both sides of the Atlantic. He states that it is now intended mainly for patients, but it is doubtful whether any but the most learned patients will plough through some of the chapters laden with references and packed with facts. Examples are the chapter on acute communicable diseases, and the chapter on cancer. Most of the text is far more suitable for the medical practitioner or student than the layman, and indeed most of the chapters make very enjoyable reading.

The most unusual—and the most amusing—chapter is the one on the history of malingering, in which Dr. Murphy shows that Dublin physicians can still write elegant and entertaining prose. Dr. Bett's own contribution on the history of appendicitis, and Dr. Balfour's edition of Sir David Wilkie's old article on gallstones, also make agreeable reading. There is a fine contribution by Dr. Lennox on the history of epilepsy, and a most interesting account of the history of pneumonia by the Brockbanks, in which they recall to us the usual treatment schedule of the disease in the twenties. Read in 1955, this seems as absurd as the women's clothes of that period.

This book is recommended as a beautifully presented and well written contribution to medical history.

FUNDAMENTALS AND APPLICATIONS OF CLINICAL OXIMETRY

W. G. Zijlstra. 150 pp. illust. 2nd revised ed. H.Fl. 12.50. Van Gorcum & Comp. N.V., Assen, 1953.

The author has brought together in one volume the various methods of photoelectric measurement of percentage oxygen saturation. The theory, construction and practical application of oximeters form the subject matter of the book.

Oximeters on this continent have been constructed almost exclusively as transmission instruments in which a vascular bed, or blood drawn from an artery, is illuminated and the light passing through measured by photoelectric means. Development in Europe, on the other hand, has been based mainly on the reflection method, in which light reflected from a skin surface or from a surface or whole blood *in vitro* is measured by similar photoelectric means. The usual point of application for the *in vivo* detector is the middle of the forehead and for this reason the oximeter is often referred to as the "cyclops."

The first half of the book is devoted to the theory and description of both the light transmission and the light reflection type of measurement. The author has relied mostly on the literature for his full but somewhat non-critical treatment of transmission oximetry. However, the development and present state of reflection oximetry which follows is given in detail and is based on intimate knowledge and experience of the subject. The advantages and disadvantages of these two principal divisions of oximetry are discussed at scattered points throughout.

The second half of the book is devoted to physiological and clinical applications of oximetry, with special reference to the Cyclops as developed by Dr. Zijlstra and his associates. The clinical applications are discussed in eight rather arbitrarily divided sections liberally exemplified with case histories, each accompanied by an oximeter record. The treatment is informal and conversational in style, with impressions and opinions freely offered.

This monograph with its many illustrations and full bibliography will provide an excellent general introduction to oximetry for those not familiar with the field. Those already familiar with transmission oximeters will find a full description of the Cyclops to round out the rather incomplete picture in most other reviews of the subject.

ENDOTHELIUM

Its Development, Morphology, Function, and Pathology. R. Altschul, Professor in Histology, University of Saskatchewan. 157 pp. illust. $3.50. The Macmillan Company, New York and Toronto, 1954.

This small monograph on endothelium contains a wealth of information on the cells lining blood vessels and lymphatics. Dr. Altschul has reviewed an amazing amount of literature, as shown by the bibliography which contains 359 entries. The literature consulted is international indeed. The book is divided into seven major chapters, the first of which concerns itself with the nomenclature; this is followed by a discussion on morphology and the development of this tissue. The growth of endothelial cells in tissue culture is discussed in a separate chapter. Metaplasia and function of endothelium take up the next two chapters. The largest chapter deals with the pathology of endothelium, and, in this field particularly, considerable emphasis is laid upon arteriosclerosis; this is understandable since the author is an authority in this particular field. Generally speaking, this book makes most instructive reading, showing how many contradictory opinions still exist in this relatively limited field of discussion and how much basic research is needed to settle some of the fundamental questions. This book should prove of great interest to anybody concerned with vascular disease and will be particularly handy as a reference to pathologists and experimental workers concerned with vascular disease. Nine figures scattered throughout the book aptly illustrate some of the points referred to by the author.

ARTHRITIS AND RHEUMATISM

C. L. Steinberg, Director of Arthritis Clinic and Senior Attending Physician in Medicine, Rochester General Hospital, and five contributors. 326 pp. illust. $10.00. Springer Publishing Company, Inc., New York, N.Y., 1954.

Interest in arthritis and allied conditions has increased in recent years. This is partly due to a better understanding of these diseases and partly to the advances in treatment which have been made. Dr. Steinberg and his colleagues endeavour to give the practising physician, who is in constant contact with arthritic and rheumatic patients, a book which he can use in his daily work. Fundamentals of physiology and pathology of arthritic, rheumatoid and collagen diseases are followed by a discussion of clinical questions from the standpoint of etiology, diagnosis, treatment and prognosis. Orthopædic procedures, physiotherapeutic methods and rehabilitation are described.

This little book is an important contribution to the medical literature, written by experts in their field. It will be welcome to the general practitioner and to those particularly interested in arthritis and rheumatism.

Canad. M. A. J.
May 15, 1955, vol. 72

INTERN'S MANUAL (Cook County Hospital)

A. Bernstein, Assistant Medical Superintendent, Cook County Hospital. 292 pp. illust. $3.00. The Year Book Publishers, Inc., Chicago; Burns & MacEachern, Toronto 2, 1954.

The Cook County Hospital, Chicago, has been in the habit of distributing mimeographed directions to its interns for some years. The fame of these notes has spread far beyond the hospital, and they are now made available as a pocket-size manual. Their chief value will be to remind the intern of the procedures he should be using in attempting to make a diagnosis of a new case, and to indicate treatment, particularly in emergencies such as postoperative complications and poisonings. There is an immense amount of information, arranged under alphabetical headings with cross-references, and it is likely that many interns will want a copy of this handy manual.

ANATOMY OF THE BRONCHOVASCULAR SYSTEM

G. L. Birnbaum, Chief, Surgical Unit, Veterans' Administration Regional Office, Portland, Oregon. 300 pp. illust. $15.00. The Year Book Publishers Inc., Chicago; Burns & MacEachern, Toronto 2, 1954.

The presence of a foreword by Dr. Evarts Graham, a revered pioneer of thoracic surgery, points to the importance of this book.

There are discussions of embryology of the tracheobronchial tree and the bronchovascular systems. Because of their brevity, it is sometimes difficult to follow the exact meaning. Many variations are described in bronchial anatomy, almost enough to discourage anyone attempting pulmonary resection, particularly segmental resection. Any surgeons interested in explaining something abnormal found at operation should be able to find it in this book. The suggested standard designation of bronchial (subsegmental) bronchi seems very complicated. There are detailed descriptions of pulmonary arteries and veins. The finer anatomy of the bronchial arteries and veins is fully described, including their communications with the pulmonary vascular system. Lymphatic drainage of the lung is fully described and good diagrams are provided.

There is a short though quite clear discussion of congenital heart anomalies, and an attempt is made to explain their occurrence on an embryological basis. This section is well illustrated, accompanied by an outline of the operative procedures indicated and contraindicated.

Various pulmonary arteriovenous fistulæ are described; excision is advised as treatment. There is a full description of various abnormal pulmonary veins and arteries, as well as the occurrence of supernumerary lobes, some of which may lie below the diaphragm. Abnormal arteries arising from a systemic source, usually the aorta, above or below the diaphragm are most important, since cutting them in this unsuspected situation may lead to fatal hæmorrhage. There is a chapter on experimental surgery of pulmonary vessels, which includes many vascular shunts, some of which have been tried clinically. This includes an outline of extra-corporeal shunts.

A review of the literature on experimental and clinical tracheobronchial surgery is given. Surgery for bronchial asthma is described, the experimental background, clinical application and results being given. In the best series, results appear to be about 50% satisfactory.

In the chapter on excision of pulmonary tissue a detailed and confusing description of abnormalities in anatomy, both vascular and bronchial, is given. In the outline of pulmonary resection techniques, approaches and operative procedures are given in bare outline, with their advantages and disadvantages. A description of the technique of segmental resection is given.

The appendix contains a series of 27 drawings of various vascular supplies within the hilum or the lung itself. Very profuse references are given at the end, to enable any interested person to go thoroughly into the subject.

This book contains a wealth of information, some of which in the reviewer's opinion is of little practical value to the surgeon. On the other hand, anyone who wishes to obtain detailed information should be able to find it here. The book appears difficult to read, partly because there are so many statements added in parentheses, but largely because an attempt is made to give a great deal of information in a very few words.

ANY QUESTIONS?

A Selection of Questions and Answers Published in the British Medical Journal. Third Series. Edited by H. Clegg. 227 pp. 7/6d. British Medical Association, London, W.C.1, 1954.

For eleven years, the expert advisers to the editor of the *British Medical Journal* have been answering questions from practitioners all over the world. Those answers of sufficient interest have been printed in the journal, and several years ago a decision was taken to make a further selection from these and reprint them in volume form. The present volume is the third of the series, and contains 200 questions and answers on subjects ranging from sedatives for sudden grief to the hazards of cellulose spraying, and the care of syringes in general practice. This volume also contains a cumulative index to all three books which have so far appeared.

FAT METABOLISM

A Symposium on the Clinical and Biochemical Aspects of Fat Utilization in Health and Disease. Edited by V. A. Najjar, Department of Pediatrics, Johns Hopkins University School of Medicine. 185 pp. illust. $4.50. The Johns Hopkins Press, Baltimore, Maryland, 1954.

This book contains papers and discussions on the clinical and biochemical aspects of fat utilization in health and disease, presented at a conference sponsored by the M. & R. Laboratories, Columbus, Ohio. Like its predecessor on carbohydrate metabolism, the book is designed to present to the clinician some of the more recent advances in the fundamental biochemistry of fat metabolism, and also to acquaint the biochemist with certain of the problems frequently encountered in clinical practice. Much of the subject matter deals with basic concepts; the book is not for the neophyte but rather for the more advanced investigator.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY

H. Bailey, Emeritus Surgeon, Royal Northern Hospital, London; General Surgeon, Metropolitan Ear, Nose and Throat Hospital: assisted by A. Clain, Senior Surgical Registrar, Royal Cancer Hospital, London. 456 pp. illust. 12th ed. $6.60. John Wright & Sons Ltd., Bristol; The Macmillan Company of Canada Limited, Toronto, 1954.

This unique and invaluable book for students first appeared in 1927. Its last edition appeared a few years ago in paperbacked sections. The latest edition is restored to its ancient glory, in keeping with the rise in standards of book production in England. No other book teaches the student so much about clinical surgical diagnosis in such an easy manner. This latest edition has undergone some revision and rearrangement, and has a new chapter on supplementary physical signs.

PROGRESS IN NEUROLOGY AND PSYCHIATRY

An Annual Review. Vol. IX. Edited by E. A. Spiegel, Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine, Philadelphia, Pa. 632 pp. $11.00. Grune & Stratton, New York; The Ryerson Press, Toronto, 1954.

This volume is the ninth under this title, published annually, in which the developments in neurology and psychiatry of the preceding year are reviewed. The review period covered currently is from December 1952 to December 1953. More than 3,700 papers dealing with work in the clinical field and related basic disciplines have been surveyed. The section on psychiatry includes a special article devoted to the most important developments in psychology in the past five years.

Sixty-nine authors have contributed to this volume, which is divided broadly into four parts: basic sciences, neurology, neurosurgery and psychiatry. The basic science section includes neuroanatomy, general and regional neurophysiology, neuropathology and the pharmacology of the nervous system.

This volume is undoubtedly useful as a reference book. It enables a neurologist or a psychiatrist, interested in recent developments in a particular subject, to find a summary of the literature of the previous year together with a very complete bibliography. Because of the wealth of material under review and the necessity for condensation, there are parts of the book where the detail given of various reports is insufficient to be of real value to the reader. There are also places where the continuity is poor and the text becomes a mere recitation of brief conclusions culled from numerous papers. In general, however, the sections are well written, and good correlation and continuity have been achieved.

One might wish that in future volumes all contributors would exercise discrimination in selecting articles for review. In this event a critical assessment of the reviewed material would not have to be limited to certain sections, as in the present volume, because of lack of space. The consequent greater uniformity in presentation should render the book as a whole more instructive and interesting to the reader. However, it can be appreciated that the literature on certain subjects is much more voluminous than is the case with others. To omit reference to many articles published during the review period might detract from the value of the book as a work of reference, which evidently is its main purpose.

PUBLIC RELATIONS IN MEDICAL PRACTICE

J. E. Bryan, Administrator, Medical-Surgical Plan of New Jersey. 301 pp. $5.00. The Williams & Wilkins Company, Baltimore, Maryland; Burns & MacEachern, Toronto, 1954.

The author, from his twenty years of association with the medical profession, has given the layman's point of view of what is wrong with public relations and medical practice and how this relationship may be corrected. There is some advantage in having someone like Mr. Bryan, who has come as close as any non-medical person to sharing the physician's viewpoint, bring to our attention as doctors those acts of word or deed which create bad relations in the eyes of the public. Often we cannot see ourselves as others see us.

This book follows a very systematic and readable pattern and describes in a series of chapters "The Doctor and His Patient . . . . His Fee . . . . His Colleagues . . . . His Community," as well as many other facets in the life of the doctor in his daily associations and work. The relationship of the physician to his various contacts, whether business or social, is the theme throughout. The book ends with a final chapter on "The Doctor and Himself," which provides some insight into the emotions and incentives which go into the practice of medicine, and which have made this profession one of the noblest of them all.

The author emphasizes the important point that the practice of medicine changes as do other aspects of our social and industrial development, and that doctors must not count on past performance but be realistic in meeting the problems they are facing today in respect to public criticism, some of which is well founded.

He points out that the medical profession is in the best position to deal with that small group of renegades among their membership who are prone to damage the reputation of the mass of conscientious doctors. He also suggests that the prime responsibility for public relations rests with each physician in the community, who must take his rightful place as healer, health expert and leading citizen in public affairs.

This book has an excellent foreword by Dr. Louis H. Bauer, Secretary General of the World Medical Association. It is a valuable reminder to the medical profession that all is not well, and is well worth reading.

CONTACT DERMATITIS

G. L. Waldbott, Senior Physician, Harper Hospital; Chief, Division of Allergy, and Physician, Grace Hospital, Detroit. 218 pp. illust. $9.75. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1953.

This book, published in 1953, has continued to attract great attention from dermatologists and allergists. It has been compiled from a series of lectures and brings to medicine an entirely new concept of the handling of the vexatious cases of contact dermatitis.

Its systematic approach to contact dermatitis progresses in a logical fashion from discussions of the mechanism involved in production up to the pathology found in these conditions. Differential diagnoses are considered, but main stress is laid upon the discovery of the causative agents. Following careful history and minute observation of contactants and environmental factors, a careful appraisal is made of the dermatological pattern arising under these conditions.

The diagrams made by superimposing line drawings on photographs are highlights of the book, and indelibly fix in the reader's mind the picture of a constant pattern arising from specific irritants.

Here is a book which gives a basic approach to the diagnosis of contact dermatitis and offers many points to the investigator for utilization. Even though it is written in scientific language, it proves to be as intriguing reading as that found in a detective novel.

This monumental work offers an approach so fundamentally sound and new that no industrial physician or specialist in this field can afford to be without it.

ABDOMINAL OPERATIONS

R. Maingot, Surgeon to the Royal Free Hospital, London, and to the Southend General Hospital. 1,580 pp. illust. 3rd ed. $24.50. Appleton-Century-Crofts, Inc., New York, 1955.

The high standard of previous editions has been maintained in this third edition of Maingot's "Abdominal Operations." The work has been entirely rewritten to bring it into line with recent surgical advances. Over four hundred new illustrations have been added, and eleven new chapters introduced.

As in previous editions, Maingot has selected a wide panel of authorities for his contributors. Each is a recognized specialist in his field and their combined efforts are in large measure responsible for the value and esteem of this volume.

If one had to select one chapter above others, that dealing with external abdominal hernia might well be

Canad. M. A. J.
May 15, 1955, vol. 72

taken. An excellent historical note has been added to previous editions. The concise manner of describing the various techniques and operations makes them readily understood. It contains the material needed for the busy practising surgeon as well as factual information for the senior student preparing for higher degrees.

To the large number of pages of the first and second editions this latest adds another three hundred—yet without becoming cumbersome. A short chapter on abdominal actinomycosis by Sir Zachary Cope is in that author's usual delightful style. Pelvic exenteration for advanced cancer in the pelvis is presented by Alexander Brunschwig. Postoperative chest complications of abdominal surgery are now considered in a chapter by themselves. A full and lucid review of fluid, electrolyte and nutritional problems is presented in a final chapter by L. P. LeQuesne.

Abdominal operations is a "must" for the serious student of surgery whether he be resident surgeon, senior student preparing for higher degrees, or the practising surgeon who wishes to keep abreast of modern advances on both sides of the Atlantic.

THE MECHANISM OF LABOUR

E. Rydberg, Professor of Obstetrics and Gynæcology, University of Copenhagen, Copenhagen, Denmark. 180 pp. illust. $5.25. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1954.

Has anyone, sitting at the receiving end of the obstetrical process, not been puzzled by the strange vagaries of the mechanism of labour? What is happening? Why? This woman has five babies born as anteriors, and here comes the sixth posteriorly—for what reason? In one woman rotation occurs at this pelvic station; in the next at one much lower—how to explain it? Professor Rydberg reviews the various theories which, by and large, are to the effect that pelvic shape determines mechanism. He then presents his own, which is that the shape and flexion of the fetal head, particularly the former, call the tune.

He demonstrates his views very convincingly with ingeniously contrived models of pelvis and fetal head. The normally shaped head, if pushed through his pelves either by hand or compressed air, rotates anteriorly; but under the same circumstances a model faithfully based on the head of a baby that moulded and delivered as a posterior, rotates posteriorly. The pelvic model remains the same, but the head shape determines the mechanism.

This book is very convincing on what actually takes place—what the mechanism of labour entails. It does not, however, tell why the moulded head that rotates posteriorly got moulded that way. It gives us the how of rotation but not the why of moulding. But we should not cavil at this half loaf. What it did for this reviewer was to clear considerably his conception of some of the factors involved in mechanism. And if he continues to sit at the perineum puzzled by the unknown—the X factor—he must be grateful to Professor Rydberg that this X does not loom quite so largely because of this valuable little book, which he wholeheartedly recommends to any obstetrician seeking light in a very dark place.

WHY WE BECAME DOCTORS

Edited by N. D. Fabricant. 182 pp. $4.00. Grune & Stratton, New York; The Ryerson Press, Toronto, 1954.

Why did you become a doctor? What a difficult question this is to answer thoroughly and honestly, when the complexity of human motivation is taken into account, and how unsatisfactory some of the answers sound. Dr. Fabricant has collected from the writings of 50 nineteenth and twentieth century physicians, ranging from Albert Schweitzer, Freud, Havelock Ellis and Somerset Maugham to less famous but nevertheless distinguished members of their profession, their views on why they chose medicine as a profession.

The first striking fact which emerges from this book is that many of the writers have not the slightest idea why they became doctors. The second is that only one comes right out in the open with the statement that medicine is "safe and practical" and therefore a sensible choice. Some, like Havelock Ellis and W. N. MacCartney, made their minds up in an instant, others had never envisaged any other career. Some were influenced by a beloved father or grandfather or family physician; others appear to have embraced medicine out of pure cussedness, in the teeth of bitter opposition. A few were stimulated by the blessed itch of scientific curiosity, while some, like Ronald Ross, had their career chosen for them.

Some of the contributions are delightful little essays in their own right, and the project as a whole is well worth study by educators and perhaps by prospective entrants to medicine.

SURGERY OF THE ŒSOPHAGUS

R. H. Franklin, Senior Lecturer and Surgeon, Post Graduate Medical School of London; Consulting Surgeon, Kingston Hospital; Late Hunterian Professor, Royal College of Surgeons. 222 pp. illust. $8.00. Edward Arnold & Co., London; The Macmillan Company of Canada Ltd., Toronto, 1952.

This relatively small volume (219 pages) brings together material on the modern advances in surgery of the œsophagus associated with the introduction of antibiotics, refinements in anæsthesia, and measures to counteract shock. A list of references at the end of each chapter is given to guide further study, and illustrations and good reproductions of radiographs are supplied. If the author had included more information on the results to be expected from the operations described, the value of the book would have been enhanced.

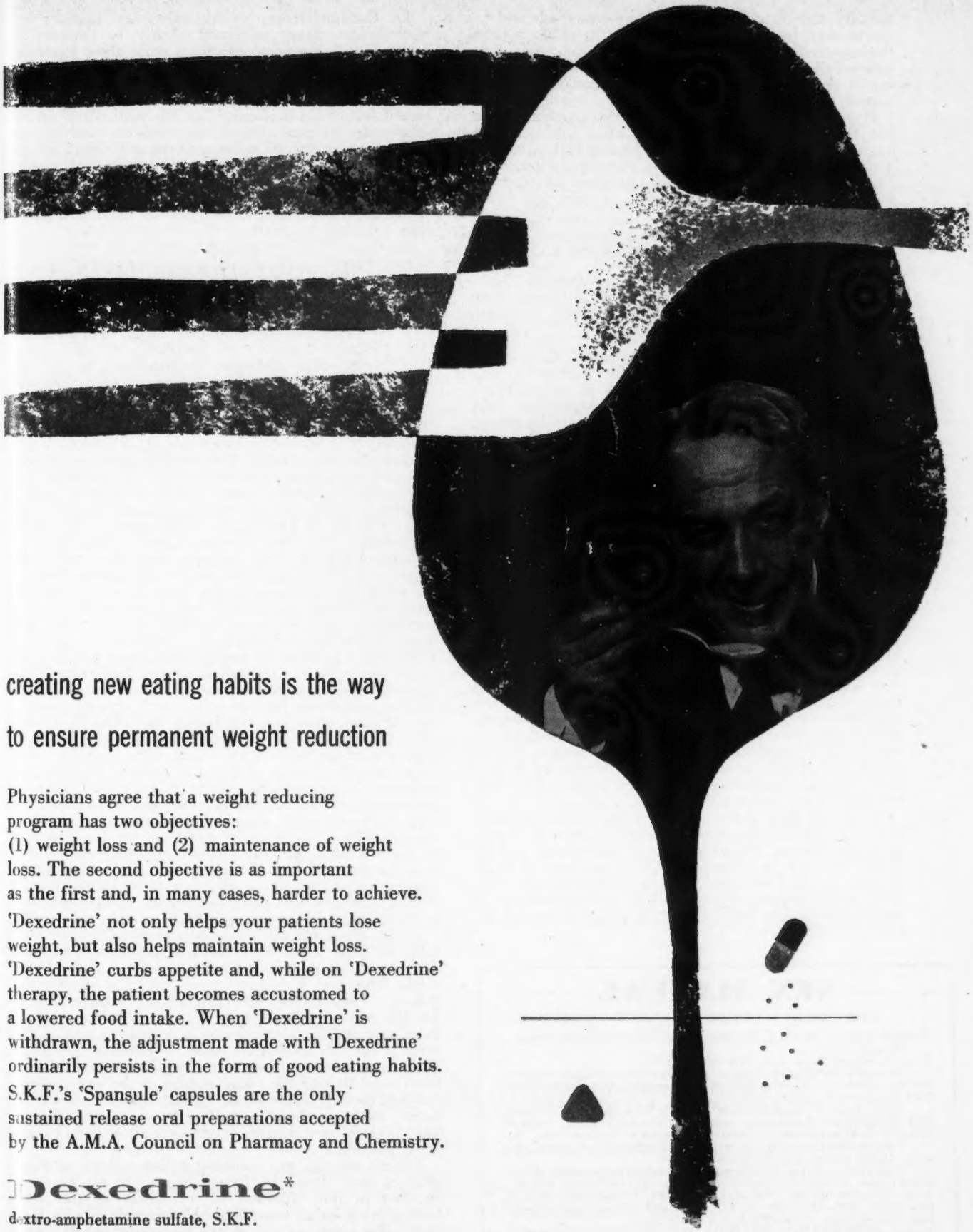
HYPNOTHERAPY IN CLINICAL PSYCHIATRY

H. Rosen. 313 pp. $5.75. The Julian Press, Inc., New York; The Copp Clark Co. Ltd., Toronto, 1953.

More than 100 years after James Braid, hypnosis remains a disputed territory. A branch of ancient knowledge, it has, for various reasons, evaded the scientific sieve and has never been fully exploited. The rise of surgical anæsthesia reduced interest in its possibilities as an analgesic agent, and the rise of psychoanalysis discredited it for many years in psychiatry. Oddly enough, it may have been the appearance of the quick-acting barbiturates, such as Evipan and thiopentone, and the narco-analytic and synthetic techniques which developed with them, that turned our attention to hypnosis again. Dr. Rosen's book is introduced by that virtuoso hypnotherapist, Dr. Milton Erickson, who has played a large part in combining dynamic psychiatry with hypnosis. Unlike certain naïve hypnotists who depend on their "glittering eye", Dr. Rosen used hypnotism as a means to an end. That end is to gain psychotherapeutic aims.

The book starts with three detailed, possibly overdetailed, case histories. This part could have been profitably shortened. The next section consists of consultation problems, mostly in general hospitals. It is excellent and internists and surgeons as well as psychiatrists should certainly read it. It deals mostly with cases seen in medical and surgical wards. The author suggests that the *grande hystérie* of Charcot is now to be found almost solely in these wards, usually in somewhat obsessional and rather depressed people.

The third section, dealing with the techniques of hypnosis, is particularly valuable to the psychiatrist. The



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Canad. M. A. J.
May 15, 1955, vol. 72

subtlety and elaboration of these new methods and the skilful way in which they are used to attain psychotherapeutically desirable ends, rather than the mere removal of symptoms, is very clearly stated. My own feeling is that this section of the book could have been usefully expanded.

Hypnosis is a valuable tool for the psychotherapist, one that has been neglected and often misused. It is no panacea, for a tool can never be any better than the hand that wields it and the mind that directs that hand. Psychiatrists, internists and surgeons could all read this book with profit.

MANIC-DEPRESSIVE DISEASE

J. D. Campbell, Diplomate, American Board of Psychiatry and Neurology. 403 pp. illust. $6.75. J. B. Lippincott Company, Montreal, 1953.

Dr. Campbell holds that manic-depressive illness arises from an imbalance of the autonomic nervous system, which disturbs the emotions and these in turn interfere with the capacity to think. He supports his views from his own observations on 522 cases in whom he discovered much evidence of autonomic disturbance.

The book needs pruning by a sympathetic editor. The case histories are long, the tabulated information is poorly presented, and figures to show the frequency of various symptoms should be given.

There are omissions, such as a mention of Kallman's work on twin studies, which is of central importance; Sheldon's body typing is almost completely ignored. Although the author is exhaustive in his account of symptoms, insomnia, one of the most important, receives no full discussion. The changes in sleep rhythm and in particular the early morning awakening are only touched on; while the tendency to morning depression and evening cheerfulness, of great diagnostic and prognostic importance, is not mentioned. Since these symptoms are very puzzling for the clinician and distressing for patients their omission is inexplicable. So also is the very small reference to amphetamine and similar euphoriants, particularly since these chemicals induce mood elevation which is sometimes followed by depression in normal people and should be discussed. The section on E.C.T. is oversimplified and does not evaluate the use of modern relaxants in any but a cursory way.

In spite of these defects, this is a very important book which all psychiatrists would do well to read. It is not, as Robert Burton, the Anatomist of Melancholy, said of chess, "for such as is students." For them, and for those training in psychiatry and for general practitioners, this book would require editing, cutting and replanning. It could only confuse and much of its real value would be lost.

Dr. Campbell's deep understanding and empathy with cyclothymes comes out most clearly in Chapter 13, which is full of wisdom and good sense about treatment. Indeed it is one of the best, most thoughtful and sympathetic accounts of caring for the mild depressive patients that I know; had the whole book reached this level it would have been a classic. This, his resounding support of the physiological view of the psychoses, and his very acute observations on manic-depressive illnesses in children, make his book one which any psychiatrist, psychoanalyst or psychotherapist ignores at his peril. It must be read critically and can hardly fail to give the reader, whatever his psychiatric persuasion, some therapeutic jolts.

THE HALLUCINOGENIC DRUGS. A NEGLECTED ASPECT OF FORENSIC MEDICINE

(The Insanity-Producing Drugs—Indian Hemp and Datura. A Loophole in the Law.) D. McI. Johnson, Barrister-at-Law. 45 pp. $1.00. Christopher Johnson, London, England; The Ryerson Press, Toronto, 1953.

This little book is a fine present for the lover of medical oddities. It is, as the reviewer sees it, a detective story with the wrong solution. The problem is to see whether one can provide a better. The story is a strange one. The author, a medical man, and his wife went mad in a hotel in 1950. He was sent to a mental hospital; she was cared for by friends. We have copies of the certificates which took him to hospital, and a letter from his solicitor about his wife. It seems that they were both suspicious, deluded and over-active. Dr. Johnson was ill for about seven days, the last three of which seem to have been spent in a state of hallucinosis and ecstasy, a condition which he says resembles intoxication with hashish. His wife recovered in a week and Dr. Johnson left hospital in about six weeks without any special treatment, although his medical attendants had warned the solicitor that he might be there for about six months.

This mysterious happening is worth careful thought. Dr. Johnson prejudices the reader by laying great emphasis on the possible use of hallucinogenic drugs by criminals, from which one might infer that he could have been the victim of such an assault. He offers no evidence to support this, although he makes much of various reports on hashish, showing that it is associated with crime. He omits to point out that the association of alcohol with crime is much more spectacular than that of hashish and, whereas hashish can only be derived from the Indian hemp, alcohol can be made from many, many hundreds of plants. He appears to exaggerate the danger of large-scale criminal drugging, though of course in these days anything is possible.

The question remains: what happened to Dr. and Mrs. Johnson? They might have had a coincidental psychosis. They might have suffered from a *folie à deux*. They might have had a pychosis produced by a vitamin deficiency. They might have taken drugs jointly. But if for the sake of argument we exclude all these, and we have very little evidence to go on, could anything else account for this misfortune, short of criminal drugging? Dr. Johnson seems to leap to the conclusion that his own illness and that of the many victims of the very sudden and unexpected outbreak of mental illness in Pont St. Esprit, France (officially ascribed to ergoty rye, though this has since been denied) might have arisen from Indian hemp poisoning.

I think we can say confidently that neither of these illnesses was caused by Indian hemp, yet we are very ignorant of the causation of an illness of this sort, lasting many days. Acute hashish poisoning usually lasts only a few hours, as also do the remarkable intoxications of mescaline, lysergic acid and ololiuqui. Dr. Johnson does point out one very important and interesting observation, that a hashish effect can be prolonged by giving the datura seeds, which contain hyoscyamine.

Although this is of great theoretical interest, it seems a little far-fetched to suppose that two poisons were present either at Pont St. Esprit or in Dr. Johnson's hotel. However, we do not need to postulate two poisons. Adrenochrome has been shown to have some effects which last for as long as 24 hours. De Jong claims that in cats indole ethylamine produced catatonic effects lasting for four days. As far as I know, we have no evidence as to what this substance will do in humans. It is, therefore, possible that certain indolic substances might, when added to food, or produced by cooking, have disastrous psychological results with very few obvious physiological results. This, I think, would be my personal solution to the problem.

Dr. Johnson is perfectly right in emphasizing that such obscure toxic conditions are very hard to diagnose. They are unlikely to receive the attention they deserve until we have more accurate means of differentiating the various sorts of excitements. Until then this fascinating story will remain a matter for speculation. But even if we cannot identify the villain with absolute certainty, this little book should be in every psychiatrist's library to tease and stimulate him in an odd hour or two.

I think we are indebted to Dr. Johnson for his courage in putting this matter into print, even though I do think his own solution is entirely mistaken.

PSYCHOMOTOR ASPECTS OF MENTAL DISEASE

H. E. King, Associate Professor of Psychiatry (Research Psychology), Tulane University School of Medicine. 185 pp. $3.85. Published for The Commonwealth Fund by Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders & Company Limited, Toronto, 1954.

This book is in itself a technical report of special rather than general interest. The author's conclusions, however, are of broad biological and humanistic significance.

Dr. King conducted an experimental study of normal, schizophrenic and neurotic people. He measured fine motor performances in tests of reactive time, tapping speed, dexterity and assembly. Chronic schizophrenes show a major psychomotor defect with retardation. The neurotic and pseudo-neurotic states show a smaller but consistent retardation. On the other hand, he found learning capacity was less altered and there was no evidence of a strong ordering factor which would be expected if the psychomotor faults were within a mechanism of mental attitude or motive. On these grounds he rejects the possibility that the defect is one of mental disorganization with faults of withdrawal, negativism and preoccupation. He suggests that the disturbance is one of a basic biological adaptation process "of motor adjustment to the external surround."

This conclusion places problems of motility and action among the problems of biological means for biological ends. The organism moves in the external environment to maintain itself and to survive. The biological apparatus serves need with action guided by the situation, and this demands an arrangement which is, at the least, sensorimotor, and with negative feedback to provide homœostatic regulation. The means need not be neural—as it is not in unicellular forms of life—but in higher orders of creatures the intermediary neural structures allow a wide range of motility for the struggle.

Many studies with this orientation press us in the direction of a holistic psychobiology. Hughlings Jackson and Goldstein as clinicians share this point of view with Sherrington, Cannon and Lashley as physiologists, and with the gestalt psychologists. Magoun and Jasper have recently demonstrated central neural processes which have diffuse connections serving general arousal and regulation of activity, and Kubie and Meninger have already pointed out that such a standpoint provides a broader frame for the facts of psycho-analytical experience.

This way of thinking of human behaviour as a study of biological capacity to adapt has great usefulness when we face mental illness, in which people are unable to do what they need to maintain themselves mentally and to survive mentally.

PERIPHERAL NERVE INJURIES

By the Nerve Injuries Committee of the Medical Research Council (Editor: H. J. Seddon). 451 pp. illust. 55/-. Her Majesty's Stationery Office, London, 1954.

This long-awaited volume summarizes the combined experiences of the British Peripheral Nerve Injury Centres during and after World War II. Much of the original and important investigative work which was published in a wide variety of journals is now gathered together in this one volume. As is inevitable in any work by several contributors, the book suffers from a certain lack of continuity and also has some notable deficiencies. For example, nowhere is there an account of ordinary nerve-suture technique. Each chapter, however, is of value in itself, and throughout the book one is impressed by the great attention paid to accurate scientific detail.

This book is a definite "must" for the libraries of orthopædic surgeons, neurosurgeons and specialists in physical medicine.

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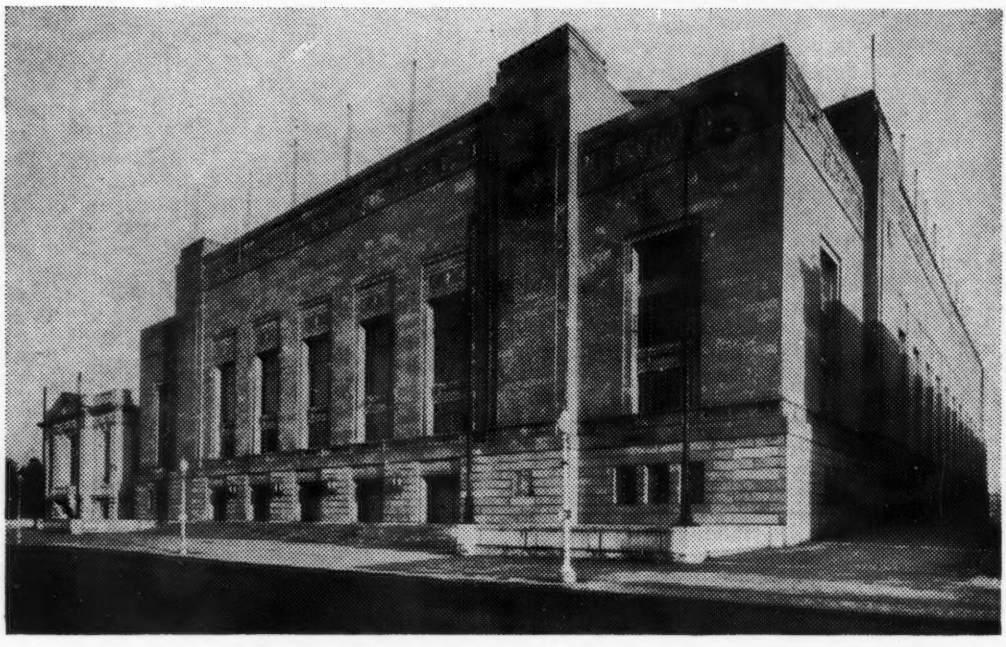

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